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EPIDEMIOLOGIC EVIDENCE ON MOBILE PHONES AND TUMOR RISK: A REVIEW

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III.B. EPIDEMIOLOGIC EVIDENCE ON MOBILE PHONES AND TUMOR RISK: A REVIEW*

ABSTRACT

This review summarizes and interprets epidemiologic evidence bearing on a possible causal relation between radiofrequency field exposure from mobile phone use and tumor risk. In the last few years epidemiologic evidence on mobile phone use and the risk of brain and other tumors of the head in adults has grown in volume, geographic diversity of study settings, and the amount of data on longer-term users. However, some key methodologic problems remain, particularly with regard to selective non-response and inaccuracy and bias in recall of phone use. Most studies of glioma show small increased or decreased risks among users, although a subset of studies show appreciably elevated risks. We considered methodologic features that might explain the deviant results, but found no clear explanation. Overall the studies published to date do not demonstrate an increased risk within approximately ten years of use for any tumor of the brain or any other head tumor. Despite the methodologic shortcomings and the limited data on long latency and long-term use, the available data do not suggest a causal association between mobile phone use and fast-growing tumors such as malignant glioma in adults (at least for tumors with short induction periods). For slow-growing tumors such as meningioma and acoustic neuroma, as well as for glioma among long-term users, the absence of association reported thus far is less conclusive because the observation period has been too short.

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Mobile phone use has increased with extraordinary rapidity, and is now nearly universal in some countries, with over two billion subscribers worldwide. The rise in use has generated concerns about safety, particularly potential cancer risk. When we reviewed this subject several years ago, we concluded that the studies at that time gave no consistent or convincing evidence of a causal relation between radiofrequency (RF) exposure and any adverse health effect. However, we could not rule out an association because of deficiencies in the research (Ahlbom et al 2004). Mobile phone studies at that time had been able to address only relatively short induction and latency periods, and included a relatively small number of heavy users. In the last five years, the volume of literature has more than doubled. We have therefore conducted a new review of the cumulated evidence on tumor risk in mobile phone users.

The emphasis of our review, and of the majority of recently published studies, is on tumors of the brain and other sites in the head that have the highest exposure from mobile phones held against the ear. These include the glial and meningeal tissue close to the surface of the head, the vestibular portion of the eighth cranial nerve where acoustic neuromas (vestibular Schwannomas) develop, and the parotid gland. For the rest of the human body the exposure is negligible except for the skin, hand and other potential sites where hands-free devices are placed. We first discuss the key methodologic issues, then review in sequence the study methods, results, and interpretation of findings for each of the cancers for which there is a substantial literature: glioma, meningioma, acoustic neuroma, and salivary glands.

III.B.1. METHODOLOGIC CONSIDERATIONS

III.B.1.1. Exposure Characteristics

The first mobile phone systems were analog and operated at 450 and 900 MHz. Digital systems, operating at higher frequencies (1,800–1,900 MHz) and using different modulation techniques, became prevalent in the early 1990s. Around 2004, third-generation systems using the Universal Mobile Telecommunication System, which operates in the 1,900–2,200 MHz frequency range, were introduced.

The systems differ also in other parameters that can influence radiofrequency exposure, including maximum power output and patterns of handovers (the manner in which the phone's connection is handed over from one base station to another). Analog systems operated at higher power levels than digital systems and probably resulted in a higher exposure per unit of use. Adaptive power control (a technology to adapt the transmission power to what is required given actual conditions, such as distance between the phone and base station) may reduce the emitted power by as much as a thousand-fold. With adaptive power control, exposure is generally higher at greater distance from the base station (e.g., in rural areas), when the user is moving (e.g., in a car), and in places where there is intensive use with frequent handovers (Hillert et al 2006; Lonn et al 2004a). To compensate for the shielding effect of building materials, power levels of phones are, on average, higher when a phone is used indoors than outdoors (Hillert et al 2006; Lonn et al 2004a). The importance of the various usage circumstances may vary with geographic location and over time (Hillert et al 2006; Lonn et al 2004a). In addition to system characteristics, the radiofrequency exposure also depends on the characteristics of the phone itself, including the type and location of the antenna (e.g., pull-out rod or built-in) and the tilt of the phone relative to the head. The spatial distribution of RF energy in the brain has been studied using measurements made on phantoms (Cardis et al 2008).4 It appears that nearly all of the energy (97-99%) is absorbed in the brain hemisphere on the side where the phone is used, mainly (50-60%) in the temporal lobe. Hands-free devices substantially reduce exposure to the head.

Most studies of mobile phones and cancer have asked the participants (or their proxies) directly about their history of use, including frequency and duration of calls. Some studies have also asked for more detail, including questions about types of phones. A few studies have instead used information on calls recorded by network operators for billing purposes. Each approach has advantages and disadvantages. More detailed data can be collected when information is obtained directly from the participants, but at the price of compromised accuracy and increased potential for recall and reporting bias. Validation

studies have shown that healthy individuals have a tendency to overestimate the length of their calls and to underestimate the frequency (Vrijheid et al 2009a; Vrijheid et al 2006). This pattern was dependent on the amount of use; heavy users tended to overestimate, whereas light users underestimated their use. A validation study including both brain tumor cases and healthy controls (Vrijheid et al 2009a) found a similar pattern among cases; however, the overestimation by cases increased with increasing time before interview, which was not seen among controls. The potential differential exposure misclassification in studies using self-reported phone use, especially for more distant time periods, may cause positive bias in estimates of disease risk. Network operator information is presumably more accurate and objective, but may be lacking in validity: some networks have information only about outgoing calls, and the information they have refers to subscribers rather than actual users. Neither self-report nor records provide all the relevant or completely accurate data. Thus, all studies based on phone use are affected by exposure misclassification, which (if non-differential) could dilute risk estimates. This is in addition to the errors inherent in inferring radiofrequency radiation exposure even from accurate information on use, for the reasons noted above.

III.B.1.2. Tumor location and laterality of tumor in relation to habitual side of phone use

When a mobile phone is held to the ear, maximum RF energy absorption occurs within the lobes of the brain or other sites near the ear that are within a few centimeters of the phone antenna. Thus, tumors in these locations are more plausibly associated with RF exposure from mobile phones than tumors at other locations.

Some case-control studies have asked about the habitual side of mobile phone use when the phone is hand-held, and have sought to investigate the association with ipsilateral and contralateral brain tumors. However, there is no evidence of consistency over time in a person's preferred side of use. Retrospective self-report of preferred side of use may be subject to bias. If cases believe that mobile phone use may have caused their tumor, they might overreport mobile phone use on the same side as the tumor. In addition, analysis of data regarding laterality of phone use presents analytic problems. First, a method is needed for handling cases and controls who say they have no preferred side of use. Second, the analysis of control data regarding laterality of mobile phone is problematic because controls have no tumor to determine a reference side. Several techniques have been employed to deal with this issue (Inskip et al 2001; Lonn et al 2004b; Takebayashi et al 2006). One should keep in mind that the one employed by Inskip et al (2001) results in a relative risk that cannot be compared with other relative risks. If a causal effect were operative, one would expect null findings for contralateral use and elevated risk for ipsilateral use, with an overall elevation in risk for all users. On the other hand, if individuals with cancer believed that phone use caused their tumor and overreport use on the affected side, this would result in an apparent excess risk of brain tumor on the side of reported phone use and a deficit in risk on the other side.

III.B.1.3. Induction and latency periods

Because mobile phones are a new technology, there is epidemiologic evidence on cancer risk only for relatively short periods since first exposure; data on exposures more than 10 years before cancer diagnosis are still limited. Most types of cancer occur many years, or even decades, after initial exposure to known carcinogens. A widely expressed view has been that it is therefore too soon to know whether mobile phones have an effect on cancer risk. However, the important issue is not how long it takes for maximum risk to occur, but how long before detectable risk is present. Even for asbestos, a carcinogen that has a notoriously long induction period, detectable elevations in risk occur 10-14 years after first exposure (Walker 1984). Futhermore, it has been argued that RF fields cannot plausibly initiate cancer since they do not damage DNA, and that if RF acts at a later stage in carcinogenesis, the effects on tumor occurrence should be relatively rapid. However, epidemiologic studies are based on diagnosed tumors, whose identification depends not just on the induction period (period between exposure and initiation of disease) but also on their latency (i.e., how long they are present before being detected). Latency is likely to be short for fast-growing malignancies, but could be decades for less-aggressive tumors such as acoustic

neuromas and benign meningiomas. Hence for glioma (or at least the subset of gliomas that are fast-growing) information on risks 10 or 15 years after first exposure could provide meaningful information for determining whether mobile phone use has an etiologic effect, although this may not be true for slower-growing tumors.

III.B.1.4. Definition of Cases

The constitution of case groups has differed across studies, in some instances in clear and logically defined ways. For example, cases may be restricted to malignant or benign tumors or defined by histologic grade or anatomic location to create the subgroup of interest. Comparison of results across studies is challenging when the diagnostic groups are overlapping but not entirely consistent. Also, the varying ways of handling attrition from the target case group of interest - eg losses due to death, inability to provide exposure or covariate information, and refusal - can be problematic methodologically.

III.B.1.5. Selection of Controls

The goal of identifying controls who are a representative sample from the population that gave rise to the cases is straightforward in principle, but it is not easily achieved in practice. For studies that identify cases comprehensively from a geographically-defined population, the desired composition of the control group is clear, although such controls are not necessarily easy to recruit and interview, as shown in two Nordic studies (Auvinen et al 2002; Lonn et al 2005). For hospital-based case-control studies, the health conditions of controls that resulted in their inclusion in the study need to be scrutinized for potential associations with mobile phone use, as seen for example in two US studies (Inskip et al 2001; Muscat et al 2000).

III.B.1.6. Response rates

Reported participation proportions have varied across studies, with inconsistent methods of calculation distorting comparisons (eTable 1). While attrition from the intended study population is fully reported in some studies, incomplete reporting makes assessment of the potential effect of selection difficult in many studies.

The cohort studies and the registry-based case-control study did not require active subject participation, allowing essentially all of the subjects to be included. Other studies required personal contact and the completion of an interview, with lower participation rates. Participation has been highest in the Scandinavian countries, with reported rates above 70% for both cases and controls in Sweden, and generally worse in other countries.

In several studies, there were indications that non-participation was related to exposure status, with mobile phone users more willing to participate than non-users (Vrijheid et al 2009b). To evaluate the potential magnitude of selection bias, most of the study centers of one study (Interphone; mentioned later) sought a short interview with non-participants (Vrijheid et al 2009b). They were able to elicit responses from 57% of control refusers and 41% of case refusers. In all centers, a lower rate of regular mobile phone use was found in controls who refused the full interview (56% overall) compared with controls who were full participants (69%), regardless of whether the study was presented as a “mobile phone” study or not. The same pattern was found for cases: 50% of case refusers were regular mobile phone users, compared with 66% among full participants. Selection bias introduced by non-participation was estimated to cause a downward bias of around 10% in odds ratios for regular mobile phone use (Vrijheid et al 2009b). It is not known if such a bias would be present differentially among various categories of users (eg between regular versus infrequent users).

III.B.1.7. Precision of risk estimates

Precision is a concern in research on rare health outcomes, which applies to all the cancers of interest here. Nonetheless, large numbers of cases have been identified for study through population registries. The other determinant of precision is the prevalence of the exposure, i.e., mobile phone use. The dramatic increase in mobile phone use over the past 20 years has implications for the power of epidemiologic studies to detect an association, with the optimal exposure prevalence for maximum power being 50%. For long-term exposure, which requires early usage given the secular trends, the numbers remain small and result in limited precision of effect estimates.

III.B.2. METHODS OF STUDIES

eTable 1 summarizes the methods of studies to date, conducted in ten countries. Aside from a group of early studies conducted in the US (Inskip et al 2001; Muscat et al 2000; Dreyer et al 1999; Muscat et al 2002; Warren et al 2003) the vast majority of publications have come from Scandinavia. One set of studies within Scandinavia was conducted by Hardell and coworkers: three on brain tumors (Hardell et al 2005a; 2006a; 2002a; 1999) and one each on salivary gland tumors (Hardell et al 2004), non-Hodgkin's lymphoma (Hardell et al 2005b), and testicular cancer (Hardell et al 2007), as well as pooled analyses of two of the brain tumor studies (Hardell et al 2006b;c). In addition, a large number of re-analyses of the brain tumor studies have been published. In this review we have considered the original publications; re-analyses were considered only if they provided relevant information not available in the original publication (Hardell et al 2002b; 2001). A third set of studies was conducted within the Interphone collaboration. Interphone consisted of a series of 16 coordinated case-control studies conducted in 13 countries. While the overall results have not been published, results of several of the national analyses (Lonn et al 2004b; Takebayashi et al 2006; Lonn et al 2005; Christensen et al 2005; Christensen et al 2004; Hepworth et al 2006; Klaeboe et al 2007; Schlehofer et al 2007; Schuz et al 2006a; Takebayashi et al 2008; Sadetzki et al 2008; Lonn et al 2006; Hours et al 2007) and pooled studies from the Nordic countries and UK (Lahkola et al 2007; 2008; Schoemaker et al 2005) have been published and are considered here. A group of independent studies the two Nordic studies (Auvinen 2002; Johansen et al 2001; Schuz et al 2006b) using subscriber data for exposure assessment and one German study (Stang et al 2001) on uveal melanoma-comprise the fourth group.

The tables in this manuscript are organized in the sequence of the preceding paragraph: Early US studies, Hardell studies, Interphone studies, and Subscriber list based studies.

Only two studies have been cohort studies (Dreyer et al 1999; Johansen et al 2001; Schuz et al 2006b) with the rest being case-control studies. All of the studies were limited to adults, although the age ranges varied somewhat. Most of the case-control studies were population-based, except for the US studies, which were hospital-based. Proxies were used to varying degrees for some of the deceased and ill cases (generally less than 10%).

The US Studies and some of the Swedish studies were based on case ascertainment that started as early as 1994, while the Interphone studies ascertained cases from 2000 through 2004. Therefore lifetime exposure prevalence among controls has varied substantially from <10% to 65%. In addition, exposure definitions and methods of categorization (ever/never use of mobile phones; definition of regular, heavy, and long-term use; and the exposure cutpoints) were inconsistent across studies, making direct comparison difficult. Tables III.B.1-5 present all the published original studies, plus published pooled analyses of the two sets of related studies (Hardell, Interphone). Pooled estimates across the overall literature are also presented. There are numerous further papers in the literature that at first sight appear to present different material but are in fact the same data analyzed in different ways or combinations. Figures 1-4 display the key results of the studies graphically. For details about the figures, refer to the footnotes in the corresponding tables.

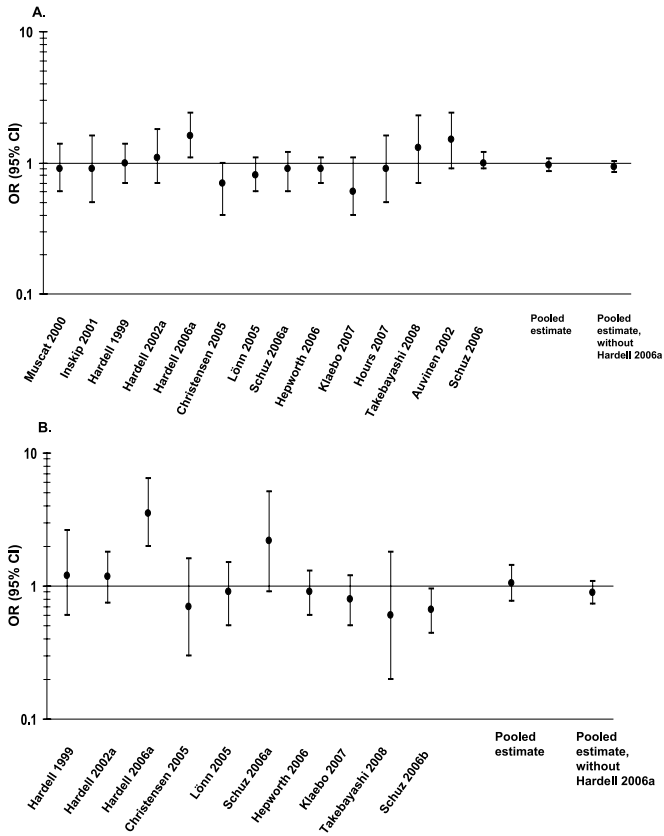

Figure III.B.1. : Mobile phone use and risk of glioma.
A, short-term use (for pooled estimate, *P* for homogeneity = 0.138; without Hardell et al (2006a) *P* = 0.443); B, long-term use (for pooled estimate, *P* for homogeneity = 0.001; without Hardell et al (2006a), *P* = 0.251.

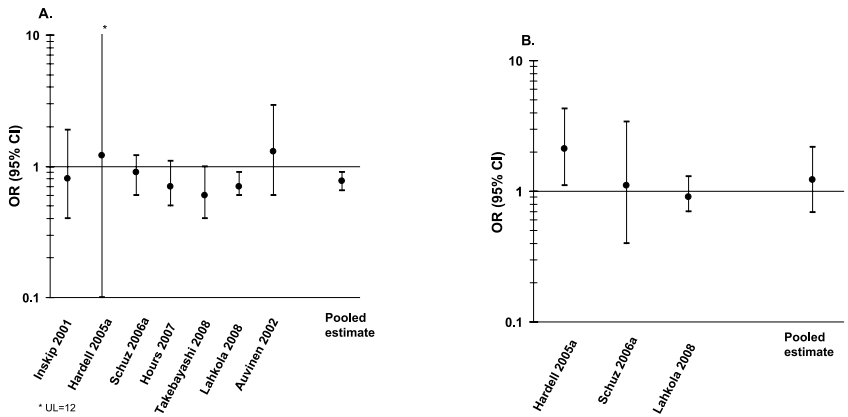

Figure III.B.2. : Mobile phone use and risk of meningioma.
A, short-term use (for pooled estimate, *P* for homogeneity = 0.602); B, long-term use (for pooled estimate, *P* for homogeneity = 0.119). * Upperlimit = 12

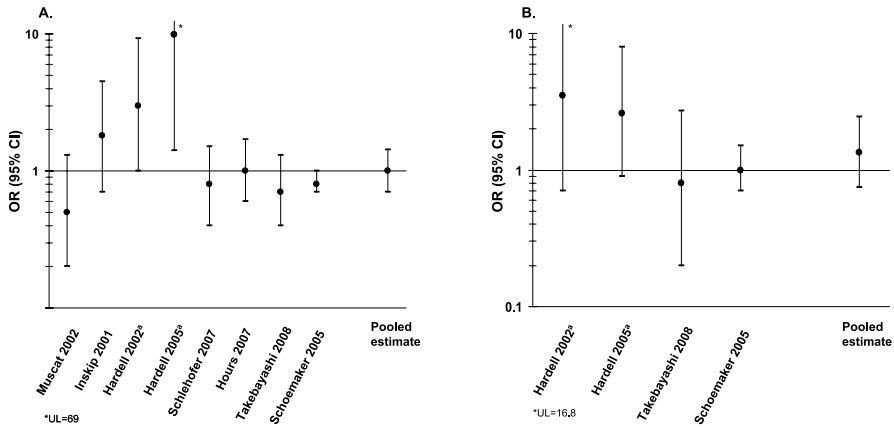

Figure III.B.3. : Mobile phone use and risk of acoustic neuroma.
A, short term use (for pooled estimate, *P* for homogeneity = 0.028); B, long term use (for pooled estimate, *P* for homogeneity = 0.191). *Upperlimit =16.8.

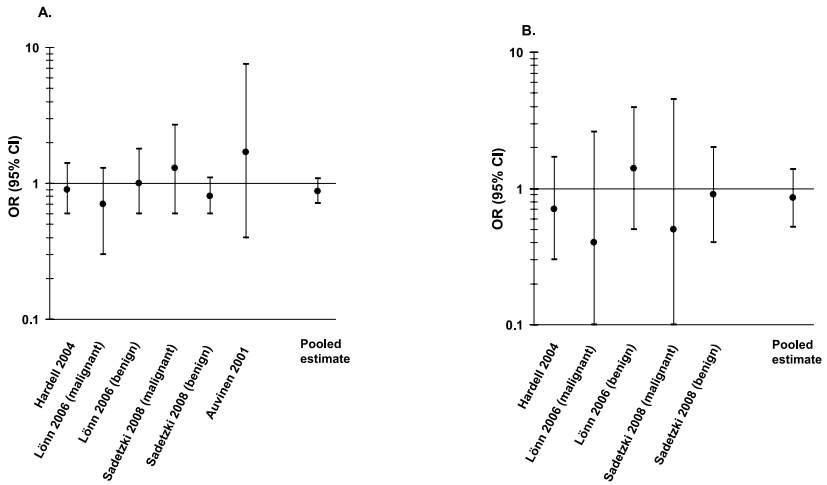

Figure III.B.4. : Mobile phone use and risk of salivary gland tumors.
A, short-term use (for pooled estimate, *P* for homogeneity = 0.667); B, long-term use (for pooled estimate, *P* for homogeneity = 0.743).

In the studies by Hardell, which provide results for both digital and analogue phones, we have chosen to present the analog results in the figures in order to avoid multiple representation and because analog phones give rise to higher exposure levels and were introduced earliest. For the Interphone group of

studies we have chosen the results by Lahkola and Schoemaker instead of the original studies for tumor types (meningioma, acoustic neuroma) where they include data that are not presented in a separate publication.

III.B.3. GLIOMA: RESULTS AND INTERPRETATION

Among the 14 original studies addressing mobile phone use and risk of glioma (Table III.B.1), most found risk estimates close to or below unity with ever-use of mobile phones (Inskip et al 2001; Lonn et al 2005; Muscat et al 2000; Hardell et al 2002a; Hardell et al 1999; Christensen et al 2005; Hepworth et al 2006; Klaeboe et al 2007; Schuz et al 2006a; Takebayashi et al 2008; Hours et al 2007; Schuz et al 2006b), while two did not (Auvinen et al 2002; Hardell et al 2006a). These two studies found risk increases after short-term exposure; Auvinen (2002) found odds ratios (ORs) ranging from 1.2 to 1.7 across indices of mobile phone exposure, with the maximum exposure category (more than 2 years of use) giving an OR of 1.7(95% CI = 0.9-3.5). The most recent study by Hardell (2006a) found increased risks in all categories of time since first use, with an OR of 1.6 (1.1-2.4) within five years based on 100 exposed cases. Hours (2007) found an OR of 2.0 (0.7-5.2) for 3.8 or more years since first use, which was the maximum exposure category analyzed in this French Interphone study. Takebayashi (2008) also reported an elevated OR after intermediate term exposure duration, but found a reduced OR after longer term exposure (more than 6.5 years). Both the Hours and Takebayashi studies included few exposed cases. For at least 10 years since first exposure, Hardell (2006a) found a more than threefold risk increase (OR = 3.6[1.7-7.5] for digital use) and Schuz (2006a) reported a twofold risk increase based on 12 exposed cases (2.2 [0.9-5.1]). Most studies, however, tended to find no evidence for an association based on duration of use or cumulative exposure (Inskip et al 2001; Lonn et al 2005; Muscat et al 2000; Hardell et al 2002a;b; Hardell et al 2001; Christensen et al 2005; Hepworth et al 2006; Klaeboe et al 2007; Schuz et al 2006b). The pooled analysis of Nordic and UK Interphone studies (Lahkola et al 2007), which to date includes the largest number of glioma cases, found an OR of 1.0 (0.7-1.2) based on 143 exposed cases, among persons who started to use a mobile phone 10 or more years prior to diagnosis. Pooling all original studies gave summary risk estimates close to unity in all exposure duration categories (OR = 1.2 [0.9-1.7] for long-term use), as well as for ever-use of mobile phones (1.0 [0.9-1.2]) (Table III.B.1). A sensitivity analysis shows that if the third Hardell et al (2006a) study were excluded, the long-term pooled OR would be 0.9 (0.8-1.1) and the heterogenity across studies would vanish (p= 0.21). This could not be achieved by, for example, excluding the Interphone studies.

Laterality of phone use in relation to laterality of tumor is a potentially important aspect of study results, but, as discussed above, there are methodologic problems with this approach. In particular, if the ipsilateral risk is raised without a raised overall risk, biased recall of side of use is implicated. Similarly, an increased ipsilateral risk together with a decreased contralateral risk also suggests that recall bias operates. This pattern is commonly found in the laterality results presented in Table III.B.2.

Lobe-specific results did not differ substantially from the corresponding overall results (Inskip et al 2001; Auvinen et al 2002; Lonn et al 2005; Muscat et al 2000; Hardell et al 2006a; Hardell et al 2002a; Schuz et al 2006b).

The overall pattern of results does not support the presence of an association between mobile telephone use and glioma. However, two issues call for clarification: (1) the basis for the discrepancy between the predominantly null findings and the few studies suggesting a positive association and (2) the tendency for studies not finding an association to report relative risks for ever-use slightly below the null value rather than dispersed symmetrically around it.

Non-differential exposure misclassification could in principle produce these negative results even in the presence of a causal effect. Might the few positive studies have resulted from a markedly superior assessment of exposure compared with studies by other investigators? The studies by Hardell et al. differed most notably in considering wireless phones in homes (DECT phones) in addition to mobile telephones (2002b; 2006a-c; 2007). However, the association between DECT phone use and glioma risk was investigated by the Swedish and German Interphone studies (Lonn et al 2005; Schuz et al 2006a;c),

without finding an increased risk of glioma. The exposure assessment methods of Auvinen et al (2002) are similar to the ones used in Schuz et al (2006b), and the methods of Schuz et al (2006a) and Hours et al (2007) are indistinguishable from those of other Interphone studies. Another potential reason for the discrepant results is selection bias through non-response among controls who did not use mobile phones, as discussed above. However, selection bias within the Interphone study was estimated to cause a downward bias in risk estimates of approximately 10% (Vrijheid et al 2009b); if this estimate is correct, this source of selection bias does not appear large enough to explain the differences in results.

If the series of negative studies is correct, it is appropriate to consider the potential reasons, including random error, for spurious positive findings in the studies generating positive results. The positive studies do not appear to have structural features with regard to case and control group constitution that would bias associations in a positive direction. The basic approach to exposure assessment does not appear to differ from that of other studies, with most studies based on self-report of use and various derived indices of exposure. While on the surface, the positive studies, including those by Hardell et al., are very much like the studies that obtained quite different results, subtle aspects of data collection and methods of analysis may be responsible for the apparent discrepancies. Investigators must make decisions regarding the exact constitution of the case groups, such as, whether to restrict by anatomic location, histology, stage, or malignancy. Exposure assignment requires even more complex decisions, including analog or digital phone use; how to define regular use; how to categorize hours of use or cumulative exposure; consideration of laterality of use and tumor location; and selection of reference dates of use for controls in relation to the timing of disease diagnosis. There is potential for differing recruitment methods to affect the magnitude and pattern of non-response, for interviewer training and monitoring to affect reporting tendencies of cases and controls, and even for the wording of questions to have subtle effects on the resulting data. Every team of investigators faces these decisions, and, presuming that there are compensating practices, the series of studies in the literature overall is expected to converge on a valid result. These decisions represent a major reason why replication of results by different research groups is needed before results can be considered as established.

The studies by Hardell and colleagues are particularly problematic because of variation across their publications in the exact constitution of case groups, criteria for exclusion, exposure definitions, and the selection of results for presentation in the multiple overlapping publications. In our view, the series of decisions in methods, analysis, and presentation provide the most plausible explanation for the deviation of the findings of the Hardell studies from those of other investigators. This does not address the other positive reports, but they seem to fit more in the distribution of results expected given random error across studies.

In summary, the complete array of available data does not suggest a causal association of mobile phone use with risk of glioma. However, there remains some uncertainty due to inconsistencies across the studies, as well as the recognized problems of exposure misclassification and potential for bias due to selective participation. As discussed previously, non-participation in the Interphone studies has been estimated to result in a 10% downward bias of the odds ratios, which can not explain all of the observed risk reduction. In addition, the period between exposure to a causal agent and manifestation of glioma may range from 5 to 20 years or more, judging from the intervals observed between ionizing radiation exposure and tumor diagnosis. Symptoms depend on the site and nature of the tumor, with slowest onset for low-grade tumors and rapid onset for highly malignant and swiftly-growing tumors. The data for long-term phone use of more than 10 years are still sparse, and any increased risk of slow-growing tumors may not yet have become manifest.

III.B.4. MENINGIOMA: RESULTS AND INTERPRETATION

Eleven original case-control studies (Inskip et al 2001; Auvinen et al 2002; Lonn et al 2005; Hardell et al 2005a; 2002a; 1999; Christensen et al 2005; Klaeboe et al 2007; Schuz et al 2006a; Takebayashi et al 2008; Hours et al 2007), one cohort study (Johansen et al 2001; Schuz et al 2006b), and two pooled analyses (Hardell et al 2006c; Lahkola et al 2008) have investigated the association between mobile phone use and meningioma. With the exception of the most recent study by Hardell (2005a), all studies

found risk estimates close to or below unity, regardless of time since first mobile phone use (Table III.B.3). The study by Hardell (2005a) found an increased risk with ever-use of an analog mobile phone (OR = 1.7 [1.0-3.0]), with the highest risk estimate for more than 10 years since first use (2.1 [1.1-4.3]). The largest study so far- the pooled analysis of the Nordic and UK Interphone studies - found an OR of 0.9 (0.7-1.3) for long term use. Pooling all original studies gave risk estimates close to or below unity (Table III.B.3). Thus, there is no consistent evidence of an increased risk of meningioma among mobile phone users.

Many of the methodologic concerns discussed above for glioma apply also to meningioma, since they were typically evaluated within the same epidemiologic studies. A particular consideration in the interpretation of studies of mengioma is the long latency for this disease. Unlike gliomas, meningiomas are typically very slow-growing tumors with probable latencies of up to 30 yrs or more (Choudhary et al 2006). Cases may have no symptoms for a long period before detection of their tumor because meningiomas compress rather than invade the brain. A proportion of patients diagnosed with meningiomas in the 1990s and included in early studies could well have had the tumor present prior to any substantive exposure to mobile phones. Thus, the negative results give weaker evidence regarding an absence of association than the corresponding negative results for glioma.

III.B.5. ACOUSTIC NEUROMA: RESULTS AND INTERPRETATION

The 13 original studies of acoustic neuroma (Inskip et al 2001; Lonn et al 2004b; Takeyabashi et al 2006; Muscat et al 2002; Warren et al 2003; Hardell et al 2005a; 2002a; 1999; Christensen et al 2004; Klaeboe et al 2007; Schlehofer et al 2007; Hours et al 2007; Johansen et al 2001; Schuz et al 2006b) (Table III.B.4) generally included small numbers of cases. The pooled analyses are larger (Hardell et al 2006c; Schoemaker et al 2005), especially the Nordic-UK pooled analysis (Schoemaker et al 2005). Response rates for cases have been relatively high, reflecting the benign nature of this tumor, but control response rates have generally been lower. For ever-use of a mobile phone, all studies found risk estimates close to or below unity, except the two most recent studies by Hardell et al (2005a; 2002a), where up to fourfold risk increases were reported. It is notable that Hardell et al (2005a; 2002a; 2006c) observed considerably increased risks also within a short time period since first use. Acoustic neuroma is a very slow-growing tumor (Thomsen et al 1990) and it seems likely that the majority of cases diagnosed within five years of their first mobile phone use would have had their tumor already present before they started to use the mobile phone. Two of the US studies (Inskip et al 2001; Muscat et al 2002) also reported somewhat elevated ORs relatively soon after first mobile phone use, but these were based on small numbers of exposed cases (Table III.B.4).

For long durations of exposure (10 years or more), the Nordic-UK pooled analysis included the largest number of cases, and reported an OR of 1.0 (0.7-1.5). Most studies found risk estimates below one, sometimes with a considerable risk reduction (eg Christensen (2004), with an OR of 0.2 [0.2-1.1], although the Swedish Interphone study (Lonn et al 2004b) found an OR of 1.9 (0.9-4-1). The two recent Hardell studies (2005a; 2002a) generated results that are discrepant from the other studies, with increased ORs of 3.5 (0.7-16.8) and 2.6 (0.9-8.0) for long-term analog phone use. Pooling all studies gave summary risk estimates of 1.2 (0.8-2.0) for long-term use, and 1.1 (0.8-1.4) for ever-use. Analyses in relation to cumulative hours of use or cumulative number of calls likewise indicated no clear associations except in one of the Hardell studies (2005a).

The risk of acoustic neuroma after reported regular ipsilateral phone use was not increased in the Nordic-UK analysis (OR 0.9 [0.7-1.1]). The same was true in the other datasets (Inskip et al 2001; Lonn et al 2004b; Takebayashi et al 2006; Muscat et al 2002; Klaeboe et al 2007; Hours et al 2007) except one by Hardell (2005a), in which there were ORs of 5.1 (1.9-14) for analog use and 2.9 (1.4-6.1) for digital use. There was, however, a raised risk associated with first ipsilateral phone use at least 10 years prior to diagnosis in the study by Lonn (OR = 3.9 [1.6-9.5]). The corresponding result in the Nordic-UK pooled analysis was 1.3 (0.8-2.0), although a raised risk was associated with at least 10 years of use (OR = 1.8 [1.0-3.3]) (Schoemaker et al 2005). Handedness has not been associated with ipsilateral tumor risk (Schoemaker et al 2005).

Acoustic neuroma can cause unilateral deafness, which could lead to cessation of phone use (and hence spuriously reduced risks). Alternatively, the deafness could lead to the diagnosis of an otherwise unrecognized tumor and hence lead to spuriously increased risks. Hearing loss associated with acoustic neuromas may influence the side of phone use as the tumor progresses, resulting in preferred contralateral phone use relative to the tumor. This is not predictable, however, since hearing can be preserved in the presence of large vestibular schwannomas and, conversely, hearing loss can frequently occur as the result of radiologically static, small tumors (Rutherford et al 2005). Potential effects on the side of mobile phone use or earlier detection of tumors should, however, affect all available studies similarly; this cannot explain the discrepancies in the results.

Unlike the situation for gliomas and meningiomas, laterality virtually defines the anatomical position of acoustic neuromas, and all ipsilateral acoustic neuromas arise close to the mobile phone handset position. Therefore if reliable unbiased information on side of exposure could be obtained, it would be possible to conduct a powerful unbiased analysis of the effect of mobile phone exposure on acoustic neuroma risk. This analysis, however, is hampered by inconsistency in side of phone use, reporting bias resulting from the tumor diagnosis, and the symptom-based changes in use noted above. The results indicating an increased risk associated with ipsilateral phone use but no overall raised risk again raise questions about the contribution of reporting bias. Thus, the elevated ipsilateral risk beyond 10 years in the large Nordic-UK analysis seems more likely to represent reporting bias than a causal effect, because the latter should lead to a raised risk (although diluted) for users overall beyond 10 years - a finding that was not seen in the overall Nordic-UK data.

As was the case for meningioma, acoustic neuromas are often present for years before diagnosis. Thus, the only data about phone use that are of any potential relevance to acoustic neuroma etiology may be the exposure occurring many years before diagnosis. The available data make it unlikely that there is any substantial raised risk of acoustic neuroma in relation to mobile phone use in the ten years preceding the diagnosis of the tumor. The results leave uncertainty as to whether there are raised risks beyond 10 years from initial use.

III.B.6. SALIVARY GLAND TUMORS: RESULTS AND INTERPRETATION

There is no consistent evidence of an increased risk of salivary gland tumors among mobile phone users (Table III.B.5, Fig. III.B.4) based on four case-control studies (Auvinen et al 2002; Hardell et al 2004; Sadetzki et al 2008; Lonn et al 2006) and one cohort study (Schuz 2006b). One study (Auvinen et al 2002) showed an increase in risk for ever-use compared with never-use and for greater cumulative years of exposure, but the results were based on few cases and had very wide confidence intervals. There was no indication of a raised risk in any of the other studies including that of Hardell. Pooling the results from all studies gave risk estimates slightly below unity in all exposure categories (Table III.B.5). Both publications from the Interphone study reported higher risk estimates associated with ipsilateral phone use at least 10 years prior to diagnosis, with an OR of 2.6 (0.9-7.9) in the Lonn study (2006), and 1.6 (0.7-3.7) in the study by Sadetzki et al (2008). Corresponding ORs for contralateral use were, however, considerably reduced in both studies: 0.3 (0.0-2.3) and 0.6 0.2-2.3), respectively. Thus, reporting bias seems likely to explain these findings.

Single studies of tumors at other sites (pituitary adenoma (Takebayashi et al 2008), non-Hodgkin's lymphoma (Hardell et al 2005b), testicular cancer (Hardell et al 2007), uveal melanoma (Stang et al 2001) are not discussed here. The main results for these cancer sites are shown in eTable 2.

III.B.7. CONCLUSIONS

In the last few years the epidemiologic evidence on mobile phone use and risk of brain and other tumors of the head has grown considerably. In our opinion, overall the studies published to date do not demonstrate a raised risk within approximately ten years of use for any tumor of the brain or any other

head tumor. However, some key methodologic problems remain - for example, selective non-response and exposure misclassification. Despite these methodologic shortcomings and the still limited data on long latency and long-term use, the available data do not suggest a causal association between mobile phone use and fast-growing tumors such as malignant glioma in adults, at least those tumors with short induction periods. For slow-growing tumors such as meningioma and acoustic neuroma, as well as for glioma among long-term users, the absence of associations reported thus far is less conclusive because the current observation period is still too short. Currently data are completely lacking on the potential carcinogenic effect of exposures in childhood and adolescence.

III.B.8. REFERENCES

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Table III.B.1.: Results of studies on mobile phone use and risk of glioma[a]

	Time since first use						Ever/never use	
	Short-term use		Intermediate-term use		Long-term use			
Reference	**No.**	**OR (95% CI)**	**No.**	**OR (95% CI)**	**No.**	**OR (95% CI)**	**No.**	**OR (95%**
US Studies								
Muscat et al 2000 (Malignant brain)	49	0.9 (0.6-1.4)[b]	17	0.7 (0.4-1.4)			66	0.7 (0.5-1.1)
Inskip et al 2001 (Glioma)	31	0.9 (0.5-1.6)	11	0.5 (0.2-1.3)			201	1.0 (0.7-1.4)
Hardell Studies								
Hardell et al 1999 (All brain)	78	1.0 (0.7-1.4)	34	0.8 (0.5-1.4)	16	1.2 (0.6-2.6)	78	1.0 (0.7-1.4)
Hardell et al 2002a,b (All	36 (analog)	1.1 (0.7-1.8)			43 (analog)	1.2 (0.8-1.8)	79 analog	1.1 (0.8-1.6)
Hardell et al 2006a (All malignant)	0 (analog)	-	20 (analog)	1.8 (0.9-3.5)	48 (analog)	3.5 (2.0-6.4)	68 analog	2.6 (1.5-4.3)
Hardell pooled analysis								
Hardell et al 2006b[c] (All malignant)	39 (analog)	1.2 (0.8-1.8)	57 (analog)	1.1 (0.8-1.6)	82 (analog)	2.4 (1.6-3.4)	178 analog	1.5 (1.1-1.9)
Interphone Studies								
Christensen et al 2005 (Glioma)[d]	43	0.7 (0.4-1.0)	42	0.6 (0.4-1.0)	14	0.7 (0.3-1.6)	106	0.7 (0.5-1.0)
Lonn et al 2005 (Glioma)	112	0.8 (0.6-1.1)	75	0.7 (0.5-1.0)	25	0.9 (0.5-1.5)	214	0.8 (0.6-1.0)
Schuz et al 2006a (Glioma)	82	0.9 (0.6-1.2)	39	1.0 (0.6-1.5)	12	2.2 (0.9-5.1)	138	1.0 (0.7-1.3)
Hepworth et al 2006 (Glioma)	271	0.9 (0.7-1.1)	170	1.0 (0.8-1.3)	66	0.9 (0.6-1.3)	508	0.9 (0.8-1.1)
Klaeboe et al 2007 (Glioma)	27	0.6 (0.4-1.1)	64	0.5 (0.3-0.8)	70	0.8 (0.5-1.2)	161	0.6 (0.4-0.9)
Hours et al 2007 (Glioma)	38	0.9 (0.5-1.6)[e]	21	2.0 (0.7-5.2)			59	1.2 (0.7-2.1)
Takebayashi et al 2008 (Glioma)	32	1.3 (0.7-2.3)[f]	17	1.9 (0.8-4.4)	7	0.6 (0.2-1.8)	56	1.2 (0.6-2.4)
Interphone pooled analysis								
Lahkola et al 2007[g] (Glioma)	384	0.8 (0.7-0.9)	342	0.8 (0.6-0.9)	143	1.0 (0.7-1.2)	867	0.8 (0.7-0.9)
Subscriber list Studies								
Auvinen et al 2002 (Glioma)	25	1.5 (0.9-2.4)[h]	11	1.7 (0.9-3.5)			36	1.5 (1.0-2.4)
Schuz et al 2006b (Nervous system)	266	1.0 (0.9-1.2)	235	1.0 (0.8-1.1)	28	0.7 (0.4-1.0)	580	1.0 (0.9-1.0)
Pooling all studies[i]		1.0 (0.9-1.1)		0.9 (0.8-1.1)		1.1 (0.8-1.4)		1.0 (0.8-1.2)
P for homogeneity		0.138		0.010		0.001		0.001

[a] All studies are case-control studies except Schuz et al 2006b
[b] Pooled result for 1 year and 2-3 years
[c] Data from Hardell 2002b and 2006a
[d] Pooled results for low grade and high grade glioma
[e] Pooled result for <1.3 years, 1.3-2.25 years, and 2.25-3.8 years
[f] Pooled result for <2.2 years and 2.2-4.7 years
[g] Data from Christensen 2005, Lonn 2005, Klaebo 2007, part of Hepworth 2006, and data from Finland not previously published
[h] Pooled result for <1 year and 1-2 years
[i] Pooling all studies except Hardell 2006b and Lahkola 2007, using the random effects model. From Hardell 2002 and 2006, when results for both analogue and digital phone use were available, only the results for analogue phone use were included to avoid including duplicate data.

OR indicates odds ratio; CI, confidence interval.

Table III.B.2.: Results of laterality analyses in studies on mobile phone use and risk of glioma

	Ever/never use		≥10 years since first use		
	Ipsilateral	Contralateral	Ipsilateral	Contralateral	
Reference	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	Comment
Hardell et al 1999/2001	1.1 (0.6-1.8)	0.7 (0.4-1.2)			
Hardell et al 2002a,b	1.9 (1.2-3.0)	0.6 (0.4-1.1)	1.8 (1.0-3.4)[a]	0.7 (0.4-1.6)[a]	Analog
	1.6 (1.1-2.4)	0.9 (0.5-1.4)	2.3 (0.6-8.9)[a]	0.3 (0.0-2.9)[a]	Digital
Hardell et al 2006a	3.1 (1.6-6.2)	2.6 (1.3-5.4)			Analog
	2.6 (1.6-4.1)	1.3 (0.8-2.2)			Digital
Lonn et al 2005	1.1 (0.8-1.5)	0.7 (0.5-1.0)	1.6 (0.8-3.4)	0.7 (0.3-1.5)	
Hepworth et al 2006	1.2 (1.0-1.5)	0.8 (0.6-0.9)	1.6 (0.9-2.8)	0.8 (0.4-1.4)	
Klaeboe et al 2007	1.0 (0.7-1.4)	0.7 (0.5-1.1)	1.3 (0.8-2.1)[b]	0.8 (0.5-1.4)[b]	
Hours et al 2007	1.2 (0.6-2.4)	1.2 (0.5-2.7)			
Takebayashi et al 2008	1.2 (0.7-2.3)	1.1 (0.6-2.0)			
Lahkola et al 2007	1.1 (1.0-1.3)	0.8 (0.6-0.9)	1.4 (1.0-1.9)	1.0 (0.7-1.4)	

[a] >6 years
[b] ≥6 years

Table III.B.3.: Results of studies on mobile phone use and risk of meningioma[a]

Reference	Time since first use: Short-term use — No. exposed cases (exposure period)	Short-term use — OR (95% CI)	Intermediate-term use — No. exposed cases (exposure period)	Intermediate-term use — OR (95% CI)	Long-term use — No. exposed cases (exposure period)	Long-term use — OR (95% CI)	Ever/never use — No. exposed cases	Ever/never use — OR (95% CI)
US Studies								
Inskip et al 2001	12 (0.5-3 years)	0.8 (0.4-1.9)	6 (≥5 years)	0.9 (0.3-2.7)			67	0.8 (0.5-1.2)
Hardell Studies								
Hardell et al 1999							16	1.1 (0.5-2.3)
Hardell et al 2002a							60 analog	1.1 (0.7-1.5)
							78 digital	0.8 (0.6-1.0)
Hardell et al 2005a	1 (analog)	1.2 (0.1-12)	14 (analog)	1.4 (0.7-2.8)	20 (analog)	2.1 (1.1-4.3)	35 analog	1.7 (1.0–3.0)
	96 (digital) (1-5 years)	1.2 (0.8-1.8)	47 (digital) (6-10 years)	1.4 (0.9-2.3)	8 (digital) (>10 years)	1.5 (0.6-3.9)	151 digital	1.3 (0.9–1.9)
Hardell pooled analysis								
Hardell et al 2006c[b]	32 (analog)	1.2 (0.8-1.8)	47 (analog)	1.2 (0.8-1.8)	34 (analog)	1.6 (1.0-2.5)	113 analog	1.3 (1.0-1.7)
	220 (digital) (1-5 years)	1.0 (0.8-1.3)	67 (digital) (6-10 years)	1.1 (0.8-1.6)	8 (digital) (>10 years)	1.3 (0.5-3.2)	295 digital	1.1 (0.9-1.3)
Interphone Studies								
Christensen et al 2005	35 (1-4 years)	0.8 (0.5-1.3)	21 (5-9 years)	0.7 (0.3-1.2)	6 (≥10 years)	1.0 (0.3-3.2)	67	0.8 (0.5-1.3)
Lonn et al 2005	64 (1-4 years)	0.6 (0.4-0.9)	40 (5-9 years)	0.7 (0.5-1.1)	12 (≥10 years)	0.9 (0.4-1.9)	118	0.7 (0.5-0.9)
Schuz et al 2006a	73 (1-4 years)	0.9 (0.6-1.2)	18 (5-9 years)	0.8 (0.5-1.5)	5 (≥10 years)	1.1 (0.4-3.4)	104	0.8 (0.6-1.1)
Klaeboe et al 2007	19 (<2 years)	0.6 (0.3-1.1)	41 (2-5 years)	0.7 (0.4-1.2)	36 (≥6 years)	1.0 (0.6-1.8)	96	0.8 (0.5-1.1)
Hours et al 2007	56 (<3.8 years)	0.7 (0.5-1.1)[c]	15 (≥3.8 years)	0.7 (0.3-1.9)			71	0.7 (0.4-1.3)
Takebayashi et al 2008	35 (<5.2 years)	0.6 (0.4-1.0)[d]	20 (>5.2 years)	1.1 (0.5-2.1)			55	0.7 (0.4-1.2)
Interphone pooled analysis								
Lahkola et al 2007[e]	286 (1-4 years)	0.7 (0.6-0.9)	214 (5-9 years)	0.8 (0.6-1.0)	73 (≥10 years)	0.9 (0.7-1.3)	573	0.8 (0.7-0.9)
Subscriber list Studies								
Auvinen et al 2002	9 ≤2 years	1.3 (0.6-2.9)[f]	2 >2 years	0.8 (0.2-3.5)			11	1.1 (0.5-2.4)
Schuz et al 2006b[3]							68	0.9 (0.7-1.1)
Pooling all studies[g]		0.8 (0.7-0.9)		0.9 (0.7-1.0)		1.2 (0.7-2.2)		0.9 (0.8-1.0)
P for homogeneity		0.602		0.799		0.119		0.232

[a] All studies are case-control studies except Schuz et al. 2006b
[b] Data from Hardell 2002a and 2005a
[c] Pooled result for <1.3 years, 1.3-2.25 years, and 2.25-3.8 years
[d] Pooled result for <1.6 years, 1.6-3.2 years, and 3.2-5.2 years
[e] Data from Christensen 2005, Lonn 2005, Klaebo 2007, and data from UK and Finland not previously published
[f] Pooled result for <1 year and 1-2 years
[g] Pooling all studies, except Hardell 2006c, Christensen 2005, Lonn 2005, and Klaebo 2007, using random effects model. From Hardell 2005, only the results for analogue phone use were included.

Table III.B.4.: Results of studies on mobile phone use and risk of acoustic neuroma[a]

Reference	Time since first use: Short-term use		Intermediate-term use		Long-term use		Ever/never use	
	No. exposed cases (exposure period)	OR (95% CI)	No. exposed cases (exposure period)	OR (95% CI)	No. exposed cases (exposure period)	OR (95% CI)	No. exposed cases	OR (95% CI)
US Studies								
Muscat et al 2002	7 (1-2 years)	0.5 (0.2-1.3)	11 (3-6 years)	1.7 (0.5-5.1)			18	0.8 (0.4-1.7)[b]
Inskip et al 2001	8 (0.5-3 years)	1.8 (0.7-4.5)	5 (≥5 years)	1.9 (0.6-5.9)			40	0.8 (0.5-1.4)
Warren et al 2003							21	1.2 (0.6-2.2)
Hardell Studies								
Hardell et al 1999							5	0.8 (0.1-4.2)
Hardell et al 2002a	12 (analog)	3.0 (1.0-9.3)	19 (analog)	3.8 (1.4-10.2)	7 (analog)	3.5 (0.7-16.8)	38 analog	3.5 (1.8-6.8)
	21 (digital) (1-5 years)	1.2 (0.6-2.2)	2 (digital) (6-10 years)	2.0 (0.2-22.1)	(>10 years)		23 digital	1.2 (0.7-2.2)
Hardell et al 2005a	2 (analog)	9.9 (1.4-69)	11 (analog)	5.1 (1.9-14)	7 (analog)	2.6 (0.9-8.0)	20 analog	4.2 (1.8-10)
	29 (digital) (1-5 years)	1.7 (0.9-3.5)	23 (digital) (6-10 years)	2.7 (1.3-5.7)	1 (digital) (>10 years)	0.8 (0.1–6.7)	53 digital	2.0 (1.1-3.8)
Hardell pooled analysis								
Hardell et al 2006c[c]	16 (analog)	2.3 (1.2-4.1)	33 (analog)	3.4 (2.1-5.5)	19 (analog)	3.1 (1.7-5.7)	68 analog	2.9 (2.0-4.3)
	75 (digital) (1-5 years)	1.4 (1.0-2.1)	29 (digital) (6-10 years)	1.8 (1.1-3.0)	1 (digital) (>10 years)	0.6 (0.1-5.0)	105 digital	1.5 (1.1-2.1)
Interphone Studies								
Christensen et al 2005	23 (1-4 years)	0.9 (0.5-1.6)	17 (5-9 years)	0.9 (0.4-1.9)	2 (≥10 years)	0.2 (0.0-1.1)	45	0.9 (0.5-1.6)
Lonn et al 2004b	44 (1-4 years)	0.8 (0.5-1.3)	30 (5-9 years)	1.1 (0.6-1.8)	14 (≥10 years)	1.9 (0.9-4.1)	89	1.0 (0.6-1.5)
Schlehofer et al 2007	20 (1-4 years)	0.8 (0.4-1.5)	8 (5-9 years)	0.5 (0.2-1.3)	0 (≥10 years)	-	29	0.7 (0.4-1.2)
Klaeboe et al 2007	4 (<2 years)	0.4 (0.1-1.4)	10 (2-5 years)	0.5 (0.2-1.2)	8 (≥6 years)	0.5 (0.2-1.4)	22	0.5 (0.2-1.0)
Hours et al 2007	44 (<3.8 years)	1.0 (0.6-1.7)[d]	14 (≥3.8 years)	0.7 (0.3-1.6)			58	0.9 (0.5-1.6)
Takebayashi et al 2008	26 (<4 years)	0.7 (0.4-1.3)	21 (4-7 years)	0.8 (0.4-1.5)	7 (≥8 years)	0.8 (0.2-2.7)	51	0.7 (0.4-1.2)
Interphone pooled analysis								
Schoemaker et al 2005[e]	231 (1-4 years)	0.8 (0.7-1.0)	96 (5-9 years)	0.9 (0.7-1.2)	31 (≥10 years)	1.0 (0.7-1.5)	360	0.9 (0.7-1.1)
Subscriber list Studies								
Schuz et al 2006b[f]							32	0.7 (0.5-1.0)
Pooling all studies[g]		1.0 (0.7-1.4)		1.3 (0.8-2.1)		1.4 (0.7-2.5)		1.0 (0.8-1.4)
P for homogeneity		0.028		0.002		0.191		0.000

[a] All studies are case-control studies except Schuz et al. 2006b
[b] Pooling of categorical analyses
[c] Data from Hardell 2002a and 2006a
[d] Pooled result for <1.3 years, 1.3-2.25 years, and 2.25-3.8 years
[e] Data from Christensen 2005, Lonn 2004b, Klaebo 2007, and data from Finland, UK-North and UK-South not previously published
[f] Nerve sheath tumours, cranial nerves
[g] Pooling all studies except Hardell 2006c, Christensen 2005, Lonn 2004b, Klaebo 2007[29], using random effects model. From Hardell 2002 and 2005 only results for analogue phone use were included.

Table III.B.5.: Results of studies on mobile phone use and risk of salivary gland tumors

Reference	Time since first use						Ever/never use	
	Short-term use		Intermediate-term use		Long-term use			
	No. exposed cases (exposure period)	OR (95% CI)	No. exposed cases (exposure period)	OR (95% CI)	No. exposed cases (exposure period))	OR (95% CI)	No. exposed cases	OR (95% CI)
Hardell Studies								
Hardell et al 2004	31 (analog) 45 (digital) >1 year	0.9 (0.6-1.4) 1.0 (0.7-1.5)	17 (analog) 8 (digital) >5 years	0.8 (0.4-1.4) 1.2 (0.5-2.8)	6 (analog) >10 years	0.7 (0.3-1.7)	31 (analog) 45 (digital)	0.9 (0.6-1.4) 1.0 (0.7-1.5)
Interphone Studies								
Lonn et al 2006	14 (malignant) 47 (benign) (1-4 years)	0.7 (0.3-1.3) 1.0 (0.6-1.8)	8 (malignant) 23 (benign) (5-9 years)	0.7 (0.3-1.7) 0.8 (0.4-1.5)	2 (malignant) 7 (benign) (≥10 years)	0.4 (0.1-2.6) 1.4 (0.5-3.9)	25 (malignant) 77 (benign)	0.7 (0.4-1.3) 0.9 (0.5-1.5)
Sadetzki et al 2008	21 (malignant) 335 (benign) (1-4 years)	1.3 (0.6-2.7) 0.8 (0.6-1.1)	11 (malignant) 246 (benign) (5-9 years)	0.9 (0.4-2.3) 1.0 (0.7-1.3)	1 (malignant) 22 (benign) (≥10 years)	0.5 (0.1-4.5) 0.9 (0.4-2.0)	33 (malignant) 252 (benign)	1.1 (0.5-2.1) 0.9 (0.6-1.1)
Subscriber list Studies								
Auvinen et al 2002	3 1-2 years	1.7 (0.4-7.5)	1 >2 years	2.3 (0.2-25.3)			4	1.3 (0.4-4.7)
Schuz et al 2006b							26	0.9 (0.6-1.3)
Pooling all studies[a] *P* for homogeneity		0.9 (0.7-1.1) 0.667		0.9 (0.8-1.1) 0.884		0.9 (0.5-1.4) 0.743		0.9 (0.8-1.1) 0.957

[a] Using random effects model. From Hardell 2004, only results for analog phone use were included.

eTable 1. Methods of studies on mobile phone use and tumor risk.

Reference	Geog. Location	Period of case ascertain.	Age Range	Hospital or population based	Tumors considered & whether histol; grade; lobe covered	Reported response rate		% proxy interviews	% exposed among controls	Comments
						Cases	Controls			
US Studies										
Dreyer et al. 1999	USA	1994	20+	Population	Total mortality					Cohort based on operator data. Follow up to Rothman 1996. Subjects using handheld phones compared to subjects using bag phones.
Muscat et al. 2000 Muscat et al. 2002	USA	1994-1998	18-80	Hospital	Malignant brain tumours (ICD9-CM codes 191.0-191.9) Lobe Grade Acoustic neuroma	75%	90%	9% brain tumor cases 1.1% AN cases 1.4% controls	18% brain tumor controls 27% AN controls (ever had a mobile phone subscription)	Data collection through personal interviews.
Inskip et al. 2001	USA	1994-1998	18+	Hospital	Glioma, Meningioma, Acoustic neuroma Grade Lobe (ICD & morph-ology codes in paper)	92%	86%	16% glioma 8% meningiom a 3% AN 3% controls	22% (regular use, i.e. at least twice per week) 45% (ever use)	Data collection through personal interviews.
Warren et al. 2003	USA	1995-2000	Not stated	Hospital	Facial nerve Acoustic neuroma	Not stated	Not stated	0%	38% (ever use)	Data collection through telephone interviews.

Hardell Studies										
Hardell et al. 1999	Sweden	1994-1996	20-80	Population	All brain tumors Malign+Benign Acoustic neuroma Grade Lobe	90%	91%	Deaths excluded	38% (at least 8 hours of use)	Response proportions exclude deaths, physician refusals from denominator in all Hardell studies. Data collection through postal questionnaires.
Hardell et al. 2002[a,b]	Sweden	1997-2000	20-80	Population	All brain tumors Malign+Benign Acoustic neuroma Grade Lobe	88%	91%	Deaths excluded	Analogue 15% Digital 30% Cordless 27% (ever use)	Repeated interviews of selected subjects; Data collection through postal questionnaires.
Hardell et al. 2005[a] Hardell et al. 2006[a]	Sweden	2000-2003	20-80	Population	Benign brain tumors Acoustic neuroma Meningioma Lobes Malignant brain tumors High grade astrocytomas	89% benign 88% malign	84%	Deaths excluded	Analogue 11% Digital 50% Cordless 44% Any type 66% (ever use)	Data collection through postal questionnaires.
Hardell et al. 2004	Sweden	1994-2000	21-80	Population	Salivary gland Also by localization and histopathology	91%	90%	Deaths excluded	Analogue 13% Digital 16% Cordless 19% Any type 33% (ever use)	Majority of controls from a 2002 brain tumor study Data collection through postal questionnaires.
Hardell et al. 2005[b]	Sweden	1999-2002	18-74	Population	Non Hodgkin Lymphoma B-cell T-cell (further subdivided) Other	91%	92%	Deaths excluded	Analogue 18% Digital 55% Cordless 41% Any type 68% (ever use)	Controls recruited on "several occasions", 30 cases excluded after ascertainment of exposure as NLH not confirmed Data collection through

										postal questionnaires.
Hardell et al. 2007	Sweden	1993-1997	20-75	Population	Testicular cancer Seminoma Non-seminoma	91%	89%	Deaths excluded	Analogue 20% Digital 16% Cordless 19% (ever use)	Data collection through postal questionnaires.
Hardell pooled analyses										
Hardell et al. 2006c Hardell et al. 2006[b]	Sweden	1997-2003	20-80	Population	Benign brain tumors Acoustic neuroma Meningioma Malignant brain tumors High grade astrocytomas			Deaths excluded		Pooled analysis of Hardell 2002[17] and 2005[15]/2006[16] No heterogeneity tests reported
<u>Interphone studies</u>										
Christensen et al. 2004 Christensen et al. 2005	Denmark	2000-2002	20-69	Population	Acoustic neuroma Meningioma Glioma Low grade, High grade (ICD & morph-ology codes in paper)	82% 71% 74%	64%	0% 2% 8%	46% 42% 50% (regular use=at least once per week during 6 months or more)	Proportion of regular use among controls reflects age and sex distribution of cases. Data collection through personal interviews.
Lonn et al. 2004[b] Lonn et al. 2005	Sweden	1999-2002 2000-2002	20-69	Population	Acoustic neuroma Meningioma Glioma Low grade, High grade Lobes (ICD & morph-ology codes in paper)	93% 84% 75%	72% 71%	0% 3% 9%	59% (regular use)	Data collection through personal interviews.

Schlehofer et al. 2007 Schuz et al. 2006[a]	Germany	2001-2003	30-69	Population	Acoustic neuroma Meningioma Glioma Low grade, High grade	89% 88% 80%	55% in AN study 63% in brain tumor study	0% 1% 11%	38% 37% 39% (regular use)	Data collection through personal interviews.
Klaeboe et al. 2007	Norway	2001-2002	19-69	Population	Acoustic neuroma Meningioma Glioma	68% 71% 77%	69%	0% 0% 36%	63% (regular use)	Data collection through personal interviews. Large proportion of interviews was made over the phone.
Takebayashi et al. 2006 Takebayashi et al. 2008	Japan	2000-2004	30-69	Hospital cases Population controls	Acoustic neuroma Meningioma Glioma Pituitary adenoma (ICD & morph-ology codes in paper)	84% 78% 59% 76%	52% 52% 53% 49%	0%	58% 52% 65% 65% (regular use)	Some hospitals did not participate. Controls selected through random digit dialing. Data collection through personal interviews.
Hepworth et al. 2006	UK	2000-2004	18-69	Population	Glioma Low grade, High grade (ICD & morph-ology codes in paper)	51%	45%	7% cases	52% (regular use)	Study includes data from two centers in the UK. Data collection through personal interviews.
Hours et al. 2007	France	2001-2003	30-59	Hospital cases Population controls	Meningioma Glioma AN	60% 78% 81%	75%	4% cases	56% (regular use)	Some hospitals did not participate. Data collection through personal interviews.
Lonn et al. 2006	Denmark and Sweden	2000-2002	20-69	Population (malignant cases and all controls) Hospital	Malignant parotid gland Benign pleomorphic adenoma	85% (Malign) 88% (Benign)	60% (Denmark) 72% (Sweden)	1 Malign case in Sweden	60% (regular use)	Matched controls in Denmark Results presented for two countries combined Data collection through

				cases (benign cases)						personal interviews.
Sadetzki et al. 2008	Israel	2001-2003	18-59	Population	Malignant and benign parotid gland histologically or cytologically confirmed	84% (Malign) 87% (Benign)	66%	4% cases 0.1 % controls	55% (regular use)	Data collection through personal interviews.
Interphone pooled analyses										
Schoemaker et al. 2005	Denmark Finland Norway Sweden UK-South UK-North	1999-2004	18-69	Population	Acoustic neuroma	83% (69-91)	51% (42-69)	0%	54% (regular use)	Age range varied by country. Pooled analysis of six Interphone studies, includes Christensen 2004, Lonn 2004, Klaeboe 2007, and data from Finland and the UK not previously published
Lahkola et al. 2007 Lahkola et al. 2008	Denmark Finland Norway Sweden UK-South	2000-2004	18-69	Population	Meningioma Glioma Glioblastoma (ICD & morph-ology codes in paper)	60% (37-81) glioma 74% (55-90) meningioma	50% (42-69)	12% of glioma cases 1.6% of meningioma 0.1% of controls	59% (regular use) 92% (ever use)	Pooled analysis of five Interphone studies, includes Christensen 2005, Lonn 2005 and Klaeboe 2007, part of Hepworth 2006, and data from Finland not previously published
<u>Subscriber list based studies and Other Studies</u>										
Auvinen et al. 2002	Finland	1996	20-69	Population	All BT Glioma,				11% (ever had a	Exposure assessment based on operator data

					Meningioma, Salivary gland Microscop Lobe				mobile phone subscription)	in case-control design
Schuz et al. 2006[b] Johansen et al. 2001	Denmark	1982-2002	18-	Population	All cancer Brain Meningioma Glioma Acoustic neuroma Salivary gland Eye, leukemia, testis Lobes				Cohort study	Exposed cohort: mobile phone subscribers. Compared to sex-, age-, and calendar year specific cancer incidence in the general Danish population. Originally published by Johansen 2001, longer follow-up analysed in Schuz 2006.
Stang et al. 2001	Germany	1995-1998	35-74	Part-hospital Part-pop.	Uveal melanoma	84% pop. 88% hosp.	48% pop. 79% hosp.	0%	<10%	

eTable 2. Results of studies on mobile phone use and risk of glioma

Reference	Diagnostic group	No. cases ever/never user	No. controls ever/never user	OR ever* *cf* never (95% CI) user	OR (95% CI) for max yrs exp. (cut point)	OR (95% CI) for max cumulative exposure	OR for ever-analogue use OR (95% CI)	Laterality (ever/never) ipsi/contra
US Studies								
Dreyer et al. 1999	Brain	2/4		No excess Too small numbers for analysis				
Muscat et al. 2000	Non-meningioma brain (mainly malignant) Astrocytic	66/403 41/313	76/346	0.7 (0.5-1.1) 0.8 (0.5-1.2)	0.7 (0.4-1.4) (≥4)	0.7 (0.3-1.4) (>480 hrs)		
Inskip et al. 2001	Glioma	201/285	358/440	1.0 (0.7-1.4)	0.6 (0.3-1.4) (≥5)	0.5 (0.2-1.3) (>500h)		Inskip method: RR=0.9, p=0.77
Hardell Studies								
Hardell et al. 1999/2001	All brain Astrocyt/glioblast	78/131 36/58	161/264	1.0 (0.7-1.4) 1.1 (0.6-1.8)	1.2 (0.6-2.6) (>10)	1.1 (0.3-3.4) (>968h)	0.9 (0.6-1.4)	1.1 (0.6-1.8)/ 0.7 (0.4-1.2)
Hardell et al. 2002[a,b]	All malignant Astrocytoma low grade Astrocytoma high grade	79 analogue 112 digital 12 analogue 16 digital 46 analogue 64 digital ? unexposed	70 analogue 99 digital 8 analogue 19 digital 37 analogue 52 digital ? unexposed	1.1 (0.8-1.6) 1.1 (0.9-1.5) 1.2 (0.8-1.9) 1.2 (0.8-1.8) 1.5 (0.6-3.7) 0.8 (0.4-1.6)	1.2 (0.8-1.8) 1.7 (0.7-4.3) (>6)		1.1 (0.8-1.6)	1.9 (1.2-3.0)/ 0.6 (0.4-1.1) (Analogue) 1.6 (1.1-2.4)/ 0.9 (0.5-1.4) (Digital)
Hardell et al. 2006[a]	All malignant	68 analogue	79 analogue	2.6 (1.5-4.3)	3.5 (2.0-6.4)	4.0 (2.2-7.3)	2.6 (1.5-4.3)	3.1 (1.6-6.2)/

		198 digital 63 unexp.	343 digital ? unexp.	1.9 (1.3-2.7)	3.6 (1.7-7.5)	2.4 (1.6-3.7)		2.6 (1.3-5.4)
	Astrocytoma low grade	5 analogue 24 digital 7 unexposed		1.2 (0.3-4.9) 1.4 (0.5-3.8)	1.2 (0.2-7.7) 1.5 (0.1-15)	1.4 (0.3-7.2) 1.8 (0.6-5.5)	1.2 (0.3-4.9)	2.3 (0.4-14)/ 0.3 (0.0-3.7)
	Astrocytoma high grade	52 analogue 129 digital 43 unexposed		3.6 (1.9-6.5) 2.2 (1.4-3.3)	4.7 (2.4-9.2) 4.5 (2.0-10) (>10)	5.7 (2.8-11) 2.7 (1.6-4.5) (>80h analogue >64h digital)	3.6 (1.9-6.5)	4.2 (1.9-9.4)/ 5.4 (2.2-13) (Analogue, similar pattern for digital)
Hardell pooled analysis								
Hardell et al. 2006[b]	All malignant	178 analogue 402 digital 322 unexp.	297 analogue 776 digital ? unexp.	1.5 (1.1-1.9) 1.3 (1.1-1.6)	2.4 (1.6-3.4) 2.8 (1.4-5.7)	5.9 (2.5-14) 3.7 (1.7-7.7) (>2000h)	1.5 (1.1-1.9)	2.1 (1.5-2.9)/ 1.1 (0.8-1.6)
	Astrocytoma low grade	5 analogue 24 digital 7 unexposed		1.2 (0.6-2.2) 1.4 (0.9-2.3)	1.6 (0.6-4.1) 1.3 (0.2-11)		1.2 (0.6-2.2)	1.8 (1.4-2.4)/ 1.0 (0.7-1.3)
	Astrocytoma high grade	52 analogue 129 digital 43 unexposed		1.7 (1.3-2.3) 1.5 (1.2-1.9)	2.7 (1.8-4.2) 3.8 (1.8-8.1) (>10)		1.7 (1.3-2.3)	(Analogue, similar pattern for digital)
<u>Interphone Studies</u>								
Christensen et al. 2005	Low grade glioma High grade glioma	47/34 59/112	90/65 155/175	1.1 (0.6-2.0) 0.6 (0.4-0.9)	1.6 (0.4-6.1) 0.5 (0.2-1.3) (≥10)	1.2 (0.5-3.1) 0.5 (0.3-1.1) (>467.9h)		
Lonn et al. 2005	Glioma Low grade glioma High grade glioma	214/157 44//29 155/117	399/275	0.8 (0.6-1.0) 0.6 (0.3-1.0) 0.9 (0.6-1.2)	0.9 (0.5-1.5) 1.0 (0.4-2.8) 0.8 (0.4-1.5) (≥10)	0.6 (0.4-1.0) 0.5 (0.2-1.1) 0.7 (0.4-1.1) (≥500h,	0.8 (0.5-1.2)	1.1 (0.8-1.5)/ 0.7 (0.5-1.0)

						handsfree adjusted)		
Schuz et al. 2006[a]	Glioma	138/ 228	283/449	1.0 (0.7-1.3)	2.2 (0.9-5.1) (≥10)	1.0 (0.6-1.6) (>195h)		
Hepworth et al. 2006	Glioma	508/456	898/818	0.9 (0.8-1.1)	0.9 (0.6-1.3) (≥10)	0.9 (0.7-1.2) (>544h)	0.9 (0.7-1.2)	1.2 (1.0-1.5)/ 0.8 (0.6-0.9)
Klaeboe et al. 2007	Glioma	161/128	227/131	0.6 (0.4-0.9)	0.8 (0.5-1.2) (≥6)	0.7 (0.4-1.3) (≥425h, handsfree adjusted)	0.7 (0.4-1.1)	1.0 (0.7-1.4)/ 0.7 (0.5-1.1)
Hours et al. 2007	Glioma	59/37	54/42	1.2 (0.7-2.1)	2.0 (0.7-5.2) (≥3.8)	1.8 (0.7-4.3) (≥260h)		1.2 (0.6-2.4)/ 1.2 (0.5-2.7)
Takebayashi et al. 2008	Glioma	56/27	106/57	1.2 (0.6-2.4)	0.6 (0.2-1.8) (>6.5)	1.7 (0.7-4.3) (>620h)	0.8 (0.2-3.0)	1.2 (0.7-2.3)/ 1.1 (0.6-2.0)
Interphone pooled analysis								
Lahkola et al. 2007	Glioma Glioblastoma	867/629 368/330	1853/1281	0.8 (0.7-0.9) 0.8 (0.6-0.9)	0.95 (0.7-1.2) 0.9 (0.6-1.2) (≥10)	0.9 (0.7-1.1) 0.9 (0.6-1.1) (>503h, handsfree adjusted)	0.9 (0.7-1.1)	1.1 (1.0-1.3)/ 0.8 (0.6-0.9)
Subscriber list based Studies								
Auvinen et al. 2002	Glioma	36/360	119/1859	1.5 (1.0-2.4)	1.7 (0.9-3.5) (>2)		2.1 (1.3-3.4)	
Schuz et al. 2006[b]	Nervous system Glioma	580 257		1.0 (0.9-1.0) 1.0 (0.9–1.1)	0.7 (0.4-1.0) (≥10)			

eTable 3. Results of studies on mobile phone use and risk of meningioma

Reference	Diagnostic group	No. cases ever/never user	No. controls ever/never user	OR ever* *cf* never (95% CI) user	OR (95% CI) for max yrs exp. (cut point)	OR (95% CI) for max cumulative exposure	OR for ever-analogue use OR (95% CI)	Laterality (ever/never) ipsi/contra
US Studies								
Inskip et al. 2001	Meningioma	67/130	358/440	0.8 (0.5-1.2)	0.9 (0.3-2.7) (≥5)	0.7 (0.2-2.4) (>500h)		Inskip method: RR=0.9, p=1.0
Hardell Studies								
Hardell et al. 1999	Meningioma	16/30	161/264	1.1 (0.5-2.3)				
Hardell et al. 2002[a]	Meningioma	60 analogue 78 digital ? unexposed	56 analogue 102 digital ? unexposed	1.1 (0.7-1.5) 0.8 (0.6-1.0)			1.1 (0.7-1.5)	
Hardell et al. 2005[a]	Meningioma	35 analogue 151 digital 103 unexposed	79 analogue 343 digital ? unexposed	1.7 (1.0–3.0) 1.3 (0.9–1.9)	2.1 (1.1–4.3) 1.5 (0.6–3.9) (>10)	2.9 (1.1–8.1) 1.5 (0.6–3.9) (>80h analogue >64h digital)	1.7 (1.0–3.0)	1.6 (0.7–3.9)/ 2.6 (1.1–6.0) (analogue) 1.5 (0.9–2.5)/ 1.5 0(.9–2.3) (digital)
Hardell pooled analysis								
Hardell et al. 2006[c]	Meningioma	113 analogue 295 digital 455 unexposed	297 analogue 776 digital ? unexposed.	1.3 (1.0-1.7) 1.1 (0.9-1.3)	1.6 (1.0-2.5) 1.3 (0.5-3.2) (>10)	1.4 (0.5-3.8) 0.7 (0.3-1.4) (>1000h)	1.3 (1.0-1.7)	1.3 (0.9-2.0)/ 1.2 (0.7-1.8) (analogue) 1.4 (1.0-1.8)/ 1.1 (0.8-1.5) (digital)

Interphone Studies								
Christensen et al. 2005	Meningioma	67/108	133/183	0.8 (0.5-1.3)	1.0 (0.3-3.2) (≥10)	0.6 (0.3-1.6) (>467.9h)	0.8 (0.5-1.3)	
Lonn et al. 2005	Meningioma	118/155	399/275	0.7 (0.5-0.9)	0.9 (0.4-1.9) (≥10)	0.7 (0.4-1.2) (≥500h, handsfree adjusted)	0.7 (0.4-1.3)	0.8 (0.5-1.1)/ 0.6 (0.4-0.9)
Schuz et al. 2006[a]	Meningioma	104/277	234/528	0.8 (0.6-1.1)	1.1 (0.4-3.4) (≥10)	1.0 (0.6-1.8) (>195h)		
Klaeboe et al. 2007	Meningioma	96/111	227/131	0.8 (0.5-1-1)	1.0 (0.6-1.8) (≥6)	0.9 (0.4-1.7) (≥425h, handsfree adjusted)	1.2 (0.7-2.3)	0.9 (0.6-1.3)/ 0.9 (0.6-1.3)
Hours et al. 2007	Meningioma	71/74	80/65	0.7 (0.4-1.3)	0.7 (0.3-1.9) (≥3.8)	0.8 (0.3-2.1) (≥260h)		0.9 (0.4-1.8)/ 0.7 (0.3-1.3)
Takebayashi et al. 2008	Meningioma	55/73	118/111	0.7 (0.4-1.2)	1.1 (0.5-2.1) (>5.2)	0.9 (0.4-2.0) (>260h)	1.1 (0.4-3.1)	1.1 (0.7-2.0)/ 0.7 (0.4-1.1)
Interphone pooled analysis								
Lahkola et al. 2007	Meningioma	573/631	1696/1249	0.8 (0.7-0.9)	0.9 (0.7-1.3) (≥10)	0.9 (0.7-1.1) (>514h, handsfree adjusted)	0.8 (0.6-1.0)	0.8 (0.7-1.0)/ 0.7 (0.5-0.8)
Subscriber list Studies								
Auvinen et al. 2002	Meningioma	11/247	48/1238	1.1 (0.5-2.4)	0.8 (0.2-3.5) (>2)		1.5 (0.6-3.5)	
Schuz et al. 2006[b]	Meningioma	68		0.9 (0.7-1.1)				

eTable 4. Results of studies on mobile phone use and risk of acoustic neuroma

Reference	Diagnostic group	No. cases ever/never user	No. controls ever/never user	OR ever* *cf* never (95% CI) user	OR (95% CI) for max yrs exp. (cut point)	OR (95% CI) for max cumulative exposure	OR for ever-analogue use OR (95% CI)	Laterality (ever/never) ipsi/contra
US Studies								
Muscat et al. 2002	AN	18/72	23/63	0.8 (0.4-1.7)*	1.7 (0.5-5.1) (3-6)	0.7 (0.2-2.6) (>60 hrs)		Inskip method: RR=0.9, p=0.07
Inskip et al. 2001	AN	40/56	358/440	0.8 (0.5-1.4)	1.9 (0.6-5.9) (≥5)	1.4 (0.6-3.4) (>100h)		Inskip method: RR=0.9, p=0.63
Warren et al. 2003	AN	21/30	53/88	1.2 (0.6-2.2)				
Hardell Studies								
Hardell et al. 1999	AN	5/8		0.8 (0.1-4.2)				
Hardell et al. 2002[a]	AN	38 analogue 23 digital ? unexposed	11 analogue 19 digital ? unexposed	3.5 (1.8-6.8) 1.2 (0.7-2.2)	3.5 (0.7-16.8) 2.0 (0.2-22.1) (>10 analogue) (>5 digital)		3.5 (1.8-6.8)	
Hardell et al. 2005[a]	AN	20 analogue 53 digital 18 unexp.	79 analogue 343 digital ? unexp.	4.2 (1.8-10) 2.0 (1.1-3.8)	2.6 (0.9-8.0) 2.7 (1.3-5.7) (>10 analogue) (>5-10 digital)	6.0 (2.2-17) 2.5 (1.2-5.2) (>80h analogue >64h digital)	4.2 (1.8-10)	5.1 (1.9-14)/ 4.9 (1.2-21) (analogue) 2.9 (1.4-6.1)/ 1.6 (0.7-3.7) (digital)
Hardell pooled analysis								

Hardell et al. 2006[c]	AN	68 analogue 105 digital 88 unexposed	297 analogue 776 digital ? unexp.	2.9 (2.0-4.3) 1.5 (1.1-2.1)	3.1 (1.7-5.7) 1.8 (1.1-3.0) (>10 analogue) (>5-10 digital)	5.1 (1.9-14) 3.1 (1.5-6.4) (>1000h)	2.9 (2.0-4.3)	3.0 (1.9-5.0)/ 2.4 (1.4-4.2) (analogue) 1.7 (1.1-2.6)/ 1.3 (0.8-2.0) (digital)
Interphone Studies								
Christensen et al. 2005	AN	45/61	97/115	0.9 (0.5-1.6)	0.2 (0.0-1.1) (≥10)	0.7 (0.3-1.7) (>467.9h)	0.3 (0.1-0.8)	
Lonn et al. 2005	AN	89/59	356/248	1.0 (0.6-1.5)	1.9 (0.9-4.1) (≥10)	1.1 (0.6-2.1) (≥450h, handsfree adjusted)	1.6 (0.9-2.8)	1.1 (0.7-1.6)/ 0.9 (0.6-1.4)
Schlehofer et al. 2006	AN	29/68	74/120	0.7 (0.4-1.2)	0.5 (0.2-1.3) (5-9)	0.4 (0.1-1.0) (>195h)		
Klaeboe et al. 2007	AN	22/23	227/131	0.5 (0.2-1.0)	0.5 (0.2-1.4) (≥6)	0.5 (0.2-1.6) (≥425h, handsfree adjusted)	0.8 (0.3-2.2)	0.7 (0.3-1.4)/ 0.9 (0.5-1.9)
Hours et al. 2007	AN	58/51	123/91	0.9 (0.5-1.6)	0.7 (0.3–1.6) (≥3.8)	0.9 (0.4-2.1) (≥260h)		0.6 (0.3-1.2)/ 1.2 (0.6-2.4)
Takebayashi et al. 2006	AN	51/46	192/138	0.7 (0.4-1.2)	0.8 (0.2-2.7) (>8)	0.7 (0.3-1.8) (>900h)	1.2 (0.4-3.8)	0.9 (0.5-1.6)/ 0.9 (0.6-1.6)
Interphone pooled analysis								
Schoemaker et al. 2005	AN	360/316	1934/1612	0.9 (0.7-1.1)	1.0 (0.7-1.5) (≥10)	0.9 (0.7-1.2) (>534h)	0.9 (0.7-1.2)	0.9 (0.7-1.1)/ 1.1 (0.9-1.4)

Subscriber list based Studies								
Schuz et al. 2006[b]	Nerve sheath tumours, cranial nerves	32		0.7 (0.5-1.0)				

* Pooling of categorical analyses

eTable 5. Results of studies on mobile phone use and risk of other tumors

Reference	Diagnostic group	No. cases ever/never user	No. controls ever/never user	OR ever* *cf* never (95% CI) user	OR (95% CI) for max yrs exp. (cut point)	OR (95% CI) for max cumulative exposure	OR for ever-analogue use OR (95% CI)	Laterality (ever/never) ipsi/contra
Hardell Studies								
Hardell et al. 2004	Salivary gland	31 analogue 45 digital ? unexposed	137 analogue 170 digital ? unexposed	0.9 (0.6-1.4) 1.0 (0.7-1.5)	0.7 (0.3-1.7) 1.2 (0.5-2.8) (>10 analogue, >5 digital)		0.9 (0.6-1.4)	
Hardell et al. 2005b	B-cell T-cell	141 analogue 422 digital 278 unexposed 14 analogue 31 digital 13 unexposed	178 analogue 559 digital 321 unexposed	0.9 (0.7-1.3) 1.0 (0.8-1.3) 1.6 (0.6-3.8) 1.4 (0.7-2.9)	1.0 (0.7-1.4) 1.1 (0.4-3.4) 1.5 (0.5-4.3) 3.0 (0.3-34.1) (>10)	1.1 (0.7-1.6) 1.1 (0.8-1.5) 1.3 (0.4-3.9) 1.5 (0.6-3.5) (>198h analogue >91h digital)	0.9 (0.7-1.3) 1.6 (0.6-3.8)	
Hardell et al. 2007	Testicular cancer	175 analogue 164 digital 515 unexposed	173 analogue 137 digital ? unexposed	1.0 (0.8–1.3) 1.1 (0.8–1.5)	2.1 (0.7–6.2) 2.8 (0.8–11) (>10 analogue, >5 digital)	0.7 (0.5–1.0) 0.9 (0.6–1.3) (>160h analogue >182h digital)	1.0 (0.8–1.3)	
Interphone Studies								
Lonn et al. 2006	Parotid, malignant Parotid, benign	25/35 77/35	401/280 202/119	0.7 (0.4-1.3) 0.9 (0.5-1.5)	0.4 (0.1-2.6) 1.4 (0.5-3.9) ≥10	0.6 (0.2-1.8) 1.0 (0.5-2.1) ≥450 hours		1.2 (0.6-2.6)/ 0.5 (0.2-1.1) 1.4 (0.9-2.2)/ 0.7 (0.4-1.1)

Sadetzki et al. 2008	Parotid, malignant Parotid, benign	33/25 252/150	88/106 603/469	1.1 (0.5-2.1) 0.9 (0.6-1.1)	0.5 (0.1-4.5) 0.9 (0.4-2.0) (≥10)	1.2 (0.4-3.5) 1.1 (0.7-1.6) (≥1035 hours)		1.0 (0.8-1.4)/ 0.9 (0.6-1.2) (malign&benign)
Takebayashi et al. 2008	Pituitary adenoma	62/39	105/56	0.9 (0.5-1.6)	0.8 (0.3-1.8) (>7.2)	1.3 (0.6-3.1) (>560h)	0.5 (0.2-1.8)	1.1 (0.7-2.0)/ 0.7 (0.4-1.1)
Subscriber list based Studies and Other Studies								
Auvinen et al. 2002	Salivary gland	4/64	18/322	1.3 (0.4-4.7)	2.3 (0.2-25.3) (>2)		1.0 (0.3-4.0)	
Schuz et al. 2006[b]	Salivary Eye Leukaemia Testis	26 42 351 522		0.9 (0.6-1.3) 1.0 (0.7-1.3)* 1.0 (0.9-1.1)* 1.1 (1.0-1.2)*	1.1 (0.7-1.5) (≥10, Leukemia)			
Stang et al. 2001	Uveal melanoma			4.2 (1.2-14.5) (ever = probable/ certain use at workplace for at least several hours per day!)				

* Pooled results for men and women