VETERANS HEALTH ADMINISTRATION
OFFICE OF PATIENT CARE SERVICES
TECHNOLOGY ASSESSMENT PROGRAM

BRIEF OVERVIEW:

HEALTH RISKS FROM CELLULAR PHONE USE

Prepared by
Karen Flynn, DDS, MS
Program Manager

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TECHNOLOGY ASSESSMENT PROGRAM

An Effective Resource for Evidence-based Managers

VA's Technology Assessment Program (TAP) is a national program within the Office of Patient Care Services dedicated to advancing evidence-based decision making in VA. TAP responds to the information needs of senior VA policy makers by carrying out systematic reviews of the medical literature on health care technologies to determine "what works" in health care. "Technologies" may be devices, drugs, procedures, and organizational and supportive systems used in health care. TAP reports can be used to support better resource management.

TAP has two categories of products directed toward filling urgent information needs of its VA clients. TAP assigns a category to each new request based on availability of studies from results of initial searches of peer-reviewed literature databases and intended use:

- The ***Brief overview*** originated as an internal memo to VA clients with both well-defined and urgent information needs. It assumes sufficient existing knowledge regarding clinical context and technology issues by its readers to omit these components of other TAP products.
- The ***Bibliography and Outline*** provide support to clients planning to conduct their own reviews.

All TAP products are reviewed internally by TAP's physician advisor and key experts in VA. Additional comments and information on this report can be sent to:

VA Technology Assessment Program • Office of Patient Care Services
Boston VA Healthcare System (11T) • 150 S. Huntington Ave. • Boston, MA 02130
Tel. (857) 364-4469 • Fax (857) 364-6587 • VATAP@va.gov

A SUMMARY FOR HTA REPORTS
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VATAP is a member of the International Network of Agencies for Health Technology Assessment (INAHTA) [www.inahta.org]. INAHTA developed this checklist© as a quality assurance guide to foster consistency and transparency in the health technology assessment (HTA) process. VATAP will add this checklist© to its reports produced since 2002.

This summary form is intended as an aid for those who want to record the extent to which a HTA report meets the 17 questions presented in the checklist. It is NOT intended as a scorecard to rate the standard of HTA reports – reports may be valid and useful without meeting all of the criteria that have been listed.

Brief Overview:
Cellular phone use
December 2009

Item	Yes	Partly	No
Preliminary			
1. Appropriate contact details for further information?	√		
2. Authors identified?	√		
3. Statement regarding conflict of interest?			√
4. Statement on whether report externally reviewed?		√	
5. Short summary in non-technical language?			√
Why?			
6. Reference to the question that is addressed and context of the assessment?	√		
7. Scope of the assessment specified?	√		
8. Description of the health technology?	√		
How?			
9. Details on sources of information?	√		
10. Information on selection of material for assessment?	√		
11. Information on basis for interpretation of selected data?	√		
What?			
12. Results of assessment clearly presented?	√		
13. Interpretation of the assessment results included?	√		
What Then?			
14. Findings of the assessment discussed?	√		
15. Medico-legal implications considered?			√
16. Conclusions from assessment clearly stated?	√		
17. Suggestions for further actions?	√		

CONTRIBUTORS TO THIS REVIEW: **No conflicts of interest.**

TAP staff person/position	Role	Responsibilities
Karen Flynn Program Manager Boston	Primary author	Conception and conduct of review: • Communication with client; • Clinical search strategy; • Interim information; • Analytic framework; • Draft review; • Final review.
Elizabeth Adams Health System Specialist Boston	Consultation throughout project	Internal content and format review.
Elaine Alligood Information Specialist Boston	Literature database searches	Database searches: • Design/conduct technical strategy; • Choose/manage databases; • Strategy text and references for report. • TAP library/archive.
Bernard Spence Administrative Officer Boston	Administrative support	• Budget/resources; • "intelligent lay reader" review; • Project tracking.
Sarah Curran Library Technician Boston	Article retrieval	Information retrieval: • Full text from print journals and electronic resources; • Manage reference lists.
Valerie Lawrence Physician Advisor San Antonio	Content and methods review	Final review: • Internal consistency, • Clarity; • clinical context; • Methods.

ABBREVIATIONS IN THIS REVIEW

AD, Alzheimer's disease

AN, acoustic neuroma

CAHTA, Catalan Agency for Health Technology Assessment (Barcelona, Spain)

CI, confidence interval

CNDS, chronic neuroimmune diseases

CNS, central nervous system

EEG, electro-encephalography

ELF-EMF, extremely low frequency electromagnetic field

EHS, electromagnetic hypersensitivity

EMF, electro-magnetic field

GP, general practitioner

IARC, International Agency for Research on Cancer

ICNIRP, International Commission for Non-Ionizing Radiation Protection

INAHTA, International Network of Agencies for Health Technology Assessment

MP, mobile phone

NS, not (statistically) significant

NOS, Newcastle-Ottawa Scale

OPCS, Office of Patient Care Services

OR, odds ratio

RCT, randomized controlled trial

RF, radio frequency

SCENIHR, Scientific Committee on Emerging and Newly Identified Health Risks (European Commission Directorate-General)

SD, standard deviation

SHR, standardized hospitalization ratio

SIR, standardized incidence ratio

SMD, standardized mean difference

TAP, Technology Assessment Program

WHO, World Health Organization

BRIEF OVERVIEW

Risk of Brain Tumors from Cellular Phone Use

OBJECTIVE

VHA's OPCS asked the Technology Assessment Program (TAP) for a review of the literature on cellular phone use. TAP approached its charge through available systematic reviews, policy statements, and technology assessments. This document will refer collectively to these synthesis publication types as "reviews".

BACKGROUND

> *"Hand-held cellular telephones were introduced to the U.S. market in 1984 but were not widely used until the mid-1990s. By early 2000, the number of subscribers had grown to an estimated 92 million in the United States and 500 million worldwide. Some concern has arisen about adverse health effects, especially the possibility that the low-power microwave-frequency signal transmitted by the antennas on handsets might cause brain tumors or accelerate the growth of subclinical tumors. It is generally agreed that the heating of brain tissue by cellular telephones is negligible, and that any carcinogenic effect would have to be mediated through a non-thermal mechanism, the nature and existence of which remain a matter of speculation. Direct genotoxic effects are unlikely."* (Inskip, 2001).

METHODS

TAP first identified available reviews. TAP then updated searches conducted by review authors to confirm the presence or absence of subsequently published eligible studies that would change review conclusions.

Search strategy/selection criteria

TAP searched Medline, the Cochrane Library, and INAHTA databases using the terms "mobile phone" and "risk", along with publication types (systematic review, meta-analysis) to identify reviews published in English from 2000 to 2009 that synthesized research in adult human patients. Searches for subsequently published review-eligible primary studies were conducted on November 23, 2009 and all searches were finally updated on December 22, 2009.

Systematic reviews (detailed below) qualify as reproducible science and require a threshold level and quality of available primary research. Hence, a catalog of published systematic reviews provides an immediately accessible overview of the general status of a body of research literature. Conversely, the lack of published reviews indicates a corresponding lack of published research.

TAP excluded:

- Narrative reviews, opinion pieces, or other publications lacking primary clinical data;
- Radiofrequency exposures other than personal cell phones;
- Laboratory or other preclinical studies;

- Articles already included in reviews;
- "Quasi-systematic" reviews, i.e., those indexed or titled as systematic but which on close examination do not meet criteria or are inadequately reported to judge: quasi-systematic reviews may attend to some details of true systematic reviews but miss their essential spirit of critical analysis.
- Unintelligibly reported articles.

One author (KF) selected citations for full-text retrieval, reviewed all articles, abstracted information, and prepared this overview with contributions from others detailed on page iii.

ANALYTIC FRAMEWORKS

Systematic reviews

Cook (1997) and Mulrow (1997) define systematic reviews: "*Systematic reviews are scientific investigations in themselves, with pre-planned methods and an assembly of original studies as their "subjects". They synthesize the results of multiple primary investigations by using strategies that limit bias and random error…"*

The same authors further specify characteristics of systematic reviews and contrast them with traditional narrative reviews: the latter synthesize articles without reporting methods of selection or quality assessment criteria and thus do not qualify as reproducible unbiased science.

Systematic reviews:

- Ask a focused clinical question;
- Conduct a comprehensive search for relevant studies using an explicit search strategy;
- Uniformly apply criteria for inclusion and exclusion of studies;
- Rigorously and critically appraise included studies;
- Provide detailed analyses of the strengths and limitations of included studies.

Systematic reviews can be quantitative (i.e., meta-analytic, applying statistical methods to summarize study results) or qualitative; in either case the inferences or conclusions of the review must follow logically from the evidence presented. The rigor of this approach is illustrated by the place of systematic reviews in evidence grading schemes (Cook 1995 and 1997; Guyatt 1995), where they receive the highest level designation. Reviews produced by the Cochrane Collaboration (www.cochrane.org) set the standard for rigor of methods and validity of conclusions, and are meta-analytic where primary studies permit. No Cochrane review group has addressed cell phone use outside of a telemedicine context.

Some reviews classified by their authors or by indexing staff as "systematic" can be less than perfectly conducted and/or reported. Grimshaw (2002) critiques such reviews for:

- ignoring methodological weaknesses in primary studies, such as unit of analysis errors (analysis of unadjusted patient data when the unit of randomization is the physician), which results in artificially extreme p values and overly narrow confidence intervals;
- use of vote-counting methods, which add up the number of positive and negative comparisons and base effectiveness conclusions on the count. Positive comparison counts fail to provide an estimate of effect size and ignore the precision of the estimates from primary studies, or fail to exclude comparisons with unit of analysis errors.

While recognizing the limitations cited above, a vote count may be the logical response of an otherwise high-quality review to heterogeneity (in research questions, methods, interventions, or outcomes) among primary studies that precludes other methods of synthesis. Conversely, use of vote counting synthesis may push an already marginal quality review frankly into the "quasi-systematic" category.

Continuum of study designs

Research on causal relationships (exposure with disease or intervention with outcome) relies on the continuum of primary research study designs shown in Table1, where designs are ranked in ascending order by strength of evidence.

Table 1: The continuum of study designs and their causal implications [Adapted from Ibrahim (1985)]

Study design	Observational	Analytic	Hypothesis-generating	Hypothesis-testing	Inference
Study designs providing only speculative inference for causation					
Anecdote	√		√		Speculative
Clinical hunch	√		√		Speculative
Case study or history	√		√		Speculative
Time series	√		√		Suggestive
Study designs providing suggestive inference					
Ecologic/ cross-sectional	√		√		Suggestive
Case-control	√	√		√	Moderately suggestive
Controlled before-after	√	√		√	Highly suggestive
Case series/historical cohort	√	√		√	Highly suggestive
Study designs allowing firm conclusions					
Prospective cohort	√	√		√	Moderately firm
RCT/community RCT		√ Experimental		√	Firm

Quality assessment for non-randomized studies

"Non-randomized studies, including case-control and cohort studies, can be challenging to implement and conduct…The Newcastle-Ottawa Scale (NOS) is an ongoing collaboration between the universities of Newcastle, Australia, and Ottawa, Canada. It was developed to assess the quality of non-randomized studies…judged on three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control and cohort studies respectively.."(Wells, 2010).

RESULTS[1]

The eight eligible reviews identified by TAP searches are outlined in Table 2 below and abstracted in detail in the Appendix. As detailed below, reviews cover 170 primary studies of cell phone use from the 1990s to the present. TAP identified very few subsequently published

[1] All figures and tables in this overview list publications in reverse chronological order by year: most recent at the top.

studies (Appendix Table 2) eligible for these reviews and none that would change review conclusions.

However, TAP abstracted in detail (Appendix Table 3) some published reports on primary associations with brain tumor from the INTERPHONE study. While subject to ongoing controversy, INTERPHONE represents the most recent and systematic efforts to resolve outstanding questions of cell phone safety. As of December 2009, final INTERPHONE results have yet to be published (IARC, 2009).

Table 2: Available reviews for cell phone use

Citation	Publication years covered	Content
Tumors		
Myung (2009)	-August 2008: 23 case–control	Any tumors
Han (2009)	-2008: 10 case-control ≥ 10 yrs	Acoustic neuroma
Kan (2008)	1966-April 2006: 9 case-control studies	Brain tumors
Other associations		
Barth (2008)	-Feb 2007: 19 experimental studies	Neurobehavioral effects
Caird (2008)	-2007: 33 studies	Driver performance
Huss (2007)	-Feb 2005: 59 studies	Source of funding and study results
SCENIHR (2007)	-2000	Possible effects on human health
Horrey (2006)	1991-2004: 23 "experiments"	Impact of phone use on driving performance
Sanchez(2001)	CAHTA assessment: Catalan with English abstract	Population health effects
Total	**8 reviews covering literature through 2008: 170 included studies (some overlap among primary studies likely**	

SUMMARY/DISCUSSION

To borrow from recent reviewers, whose conclusions have not been changed by subsequently published research or over much of the past decade:

> *"Studies published to date cannot adequately determine whether cell phone use or other exogenous environmental factors such as increasing noise may have contributed to the increasing rates of AN. In 1997, the International Agency for Research on Cancer (IARC) coordinated an international collaborative case-control study on cell phone use and the incidence of brain tumors in 13 countries (the INTERPHONE study;* Appendix Table 3*). All of these studies relied on self-reported cell phone use through various questionnaires. The results of these studies remain controversial, in part, because most suffer from various methodological deficiencies including insufficient statistical power to detect an excess risk of brain tumors, reliance on small populations, short-term exposure periods, and difficulty in characterizing changing exposures throughout a lifetime in large populations. In addition, most negative studies have been substantially funded by the cell phone industry."* (Han, 2009).
>
> *"Nine case-control studies containing 5,259 cases of primary brain tumors and 12,074 controls were included* (in a systematic review with meta-analysis). *All studies reported ORs according to brain tumor subtypes, and five provided ORs on patients with ≥ 10*

> *years of follow up. Pooled analysis showed an OR of 0.90 (95% confidence interval [CI] 0.81-0.99) for cellular phone use and brain tumor development. The pooled OR for long-term users of ≥ 10 years (5 studies) was 1.25 (95% C, 1.01-1.54). No increased risk was observed according to analog or digital phone use…We found no increased risk of brain tumors among cellular phone users. The potential elevated risk of brain tumors after long-term cellular phone use awaits confirmation by future studies."* (Kan, 2008).
>
> *"It is too soon for a verdict on the health risks from cellular telephones, especially in view of changing technology. From the Interphone Study and some other large studies in progress, better information may emerge. From the epidemiological information available now, the main public-health concern is clearly motor vehicle collisions, a behavioral effect rather than an effect of radiofrequency exposure as such. Neither the several studies of occupational exposure nor the few of cellular telephone users offer any clear evidence of an association with brain tumors or other malignancies. Even if the studies in progress were to find large relative effects for brain cancer, the absolute increase in risk would probably be much smaller than the risk stemming from motor vehicle collisions. Cellular telephones affect quality of life in myriad ways, for good and ill; the health risk is just one part of a picture that is slowly coming into focus."* (Rothman, 2000).

The literature on cell phone safety is controversial and inconclusive, hampered by the relatively short history of phones, difficulties precisely quantifying exposures, changing technology, confounding environmental or occupational sources of radiation, and industry funding. Phones ultimately may not be demonstrated to be completely safe, but neither is it likely that their close integration into daily activities by much of the human population will permit foregoing use in absence of an alternative:

> *"Ultimately the perception of safety will be heavily influenced by the perceived level of benefit from the activity in question. This level is clearly high in the case of mobile telephones and in many other domains where individuals exercise freedom of choice. …an editorial in the* ***Guardian*** *in 1977…an inquiry into a cluster of explosions of domestic gas:" Whatever the findings, gas will not become safe. Some oaf will always leave a tap on and then go down at the dead of night with a lighted taper". This highly explosive substance is piped into millions of homes in the country. Is it safe? Of course not, but the amenity value is such that people are prepared to live with the risk. Researchers into the pursuit of safety, of mobile phones or other features of modern living, would be well advised to take this political element into consideration."* (Dendy 2000).

It may be useful to consider cell phone exposure research in context with the early cigarette/lung cancer literature: the magnitude of risk with phones [best estimate non-significant odds ratio (OR), 0.7 from the Danish cohort: Appendix Table 3) is certainly less than that for tobacco (OR, approximately 10) and will be difficult to prove with certainty lacking the natural experiment available in the 1950s, when the first tobacco hazards research was conducted among British physicians (Lilienfeld and Stolley, 1994).

To summarize: any link between cell phone use and disease has yet to be definitively demonstrated and any risk quantified. Several factors (human, politico-cultural, technological) argue against imminent resolution of the issues or subsequent change in human behavior although the INTERPHONE Study (Appendix Table 3) final results are pending publication.

The single most rigorous study available (Schüz, 2006 and 2009; Johansen, 2001: Appendix Table 2), a population cohort, found no association between cell phone use and a variety of

cranial tumors in comparing all private cell phone subscribers in Denmark versus the entire population during twenty years of follow-up.

Finally, concluding a report on the absence of time trends in brain tumor incidence from four Nordic countries, Deltour (2009; Appendix Table 2) lays out possible explanations:

> *"The lack of a detectable trend change in incidence rates up to 2003 in this study suggests that the induction period for brain tumors associated with mobile phone use exceeds 5-10 years, that the increased risk of brain tumors associated with mobile phone use in this population is too small to be observed, that the risk is restricted to subgroups of brain tumors, or there is no increased risk associated with mobile phone use. Because of the high prevalence of mobile phone exposure in this population and worldwide, longer follow-up of time trends in brain tumor incidence rates are warranted."* Deltour (2009).

APPENDIX

Table 1: reviews for cellular phone use

Citation	Objective/Methods	Results, Conclusions, Recommendations, Comments
Han (2009)	**Cell phone use and AN risks:** • PubMed, -2008; • "Published articles" on association between cell phone use and AN/other brain tumors.	**12 articles:** • 1 cohort study; 10 case-controls; 1 meta-analysis; • Benign brain tumors: 2 US case-control with phone use < 10 yrs found NS association with AN; • Study limitations: lack of precision for changes in cell phone use over time; short exposure periods; inability to evaluate patterns of use consistent with the contemporary. **Conclusions:** *"The evaluation of AN risk factors is challenging due to its long latency. Some studies of longer term cell phone use have found an increased risk of ipsilateral AN. Adopting a prospective approach to acquire data on cell phone use, obtaining retrospective billing records that provide independent evaluations of exposure, and incorporating information on other key potential risk factors from questionnaires could markedly advance the capacity of studies to evaluate the impact of cell phones on AN."*
Myung (2009)	**To investigate by meta-analysis inconsistent findings from case-control studies on the association between cell phone use and tumor risk:** • Multiple databases to August 2008; • Included: case-control studies of cell, mobile, or cordless phone exposure and benign or malignant tumors reporting results as adjusted ORs with CIs; • Excluded: duplicate publications from same study; • Quality assessment by NOS scale; • Main analysis: Use vs non - or rare use and overall risk of all tumors; • Subgroup analyses: status as case or control blinded at interview; adjusted vs crude incidence data; overall methodologic quality; type of tumor; analog or digital phone; hospital or population case-control; long term use (≥ 10 years).	**23 studies:** • 37,916 subjects (12,344 cases; 25,572 controls); • Mean age, 52.6 yrs (18-90); 51% female; • Reported phone use, 43.5% of cases; 45.2% of controls; • Use Vs non-use not significantly associated with tumor risk overall (OR, 0.98; CI, 0.89-1.07); but positive/harmful association in blinded studies (9/15 from Interphone; OR, 0.85; CI, 0.80-0.91); without publication bias; • Range of quality scores: 5-8; mean, 6.3; • Subgroup analysis by research group: significant positive association in Swedish studies (not reported separately here as included in reviews); and significant negative association for Interphone studies; • Subgroup for crude data use: no significant association in any included study; • No significant findings for type of tumor (anatomy, malignant or benign) or type of phone. **Conclusions:** *"The current study found that there is possible evidence linking mobile phone use to an increased risk of tumors from a meta-analysis of low-biased case-control studies. Prospective cohort studies providing a higher level of evidence are needed."*

Citation	Objective/Methods	Results, Conclusions, Recommendations, Comments
Barth (2008)	**To clarify equivocal results: effects of EMFs emitted by cell phones:** • PubMed to Feb 28 2007; • Included in meta-analysis: treatment (phone switched on vs control (phone off) single- or double-blind comparisons; mean and SD or test statistics for dependent variables at two time points reported; phones emitting 900 MH to 1800 MH used by healthy subjects; standardized neuropsychological outcome measure reported.	**10 included studies:** • Decreased reaction time by subtraction test; • Working memory (N-back test) affected; • Number of errors (2-back) higher in exposed subjects. **Conclusions*: "****EMFs may have small effects on human attention and working memory."*
Caird (2008)	**Effects of phone use on driving performance:** • Multiple databases -2007; • Studies reporting: dependent variables (reaction time, headway, speed, lateral control); methodologic details (statistical information, null results, post hoc tests).	**33 studies with 2000 subjects:** • Overall mean decrease (0.25 seconds) in reaction time with phone-related tasks, probably underestimating true behavior of drivers in their own vehicles; • Drivers do not appreciably compensate for phone use by greater headway or reduced speed; • No statistically significant differences by setting (on-road/highway or laboratory simulation). **Conclusions:** *"…cell phone conversation while driving reduces reaction time to events and stimuli...unequivocal in this meta-analysis and consistent with previous meta-analyses. The estimates for effect on reaction time range from .460-.546…Hand-held and hands-free phones produced similar mean performance decrements. This result has important implications for legislative restrictions and vehicle and device manufacturers of hands-free in-vehicle systems."*
Kan (2008)	**Effects of cell phone use on risk of brain tumor development:** • Medline, 1966-April 2006; • "All relevant articles" on cell phone use; • Included: English-language case-control studies from which ORs could be calculated and exposure levels were clearly defined; • Excluded: studies of exposure other than cell phones (e.g., cordless phones); case reports or series.	**10 case-controls:** • 2000-2006; • 5,259 cases; 12,074 controls; • 5 studies reported ORs by tumor subtypes; 5 studies by ≥ 10 years follow-up; • Pooled analysis: OR 0.90 (CI, 0.81-0.99) for phone use and tumor development; ≥ 10 yrs use: OR1.25 (CI, 1.01-1.54); • No differential increased risk analog Vs digital phones. **Conclusions:** *"We found no overall increased risk of brain tumors among cellular phone users. The potential elevated risk after long term use awaits confirmation by future studies."*
Huss (2007)	**Is industry involvement associated with results and methodologic quality of studies?** • Embase and Medline to Feb 2005; • Reporting effects of controlled exposure (WHO "human laboratory studies") in English, French, or German;	**59 studies:** • 12 (20%) funded exclusively by industry, 11(19%) public or charity, 14 (24%) mixed, 22 (37%) not reported; • Industry-funded studies addressed largest number of outcomes but were least likely to find statistically significant association.

Citation	Objective/Methods	Results, Conclusions, Recommendations, Comments
	• Exposure to radiofrequency radiation on health-related outcomes (EEG recordings; assessments of cognitive or cardiovascular function; hormone levels; subjective well-being and symptoms); • Excluded: risks of phone use while driving or operating machinery; EMF incompatibilities (pacemakers or hearing aids); telemedicine applications (phones for monitoring of or communication with patients); • Data for logistic regression: source of funding (industry, public or charity, mixed, not reported); potential confounders [study design, exposure (frequency, duration, intensity)]; methodologic or reporting quality (study design, allocation concealment, blinding); • Primary outcome: at least one statistically significant ($p<0.05$) association between exposure and outcome.	**Conclusions:** *"Most (68%) of the studies assessed here reported biologic effects. At present it is unclear whether these biologic effects translate into relevant health hazards. Reports from national and international bodies have recently concluded that further research efforts are needed, and dedicated research programs have been set up in the United States, Germany, Denmark, Hungary, Switzerland, and Japan. Our study indicates that the interpretation of results from existing and future studies of the health effects of radiofrequency should take sponsorship into account."*
SCENIHR (2007)	**Update to 2001 opinion:** • English-language post-2000 peer-reviewed studies (clinical or laboratory); • Addressing EMF association with disease; • Studies in other languages considered if significant contribution.	**Opinion:** **Radiofrequency fields:** *"The additional information which has become available on carcinogenic and other non-thermal effects of radiofrequency and microwave frequencies does not justify a revision of 1998 exposure limits. In particular, in humans, no evidence of carcinogenicity in either children or adults has resulted from epidemiologic studies (some of which were very large although not for long enough observation periods for definitive statements). A relatively large series of laboratory studies has not provided evidence of genetic toxicity. Subjective symptoms affecting some individuals possibly exist, but not enough information is available on: the levels of exposure producing such an effect; the features underlying individual susceptibility; or the prevalence of susceptible individuals in different populations. Thus, current knowledge is insufficient for the implementation of measures aimed at the identification and protection of a highly sensitive subgroup of the population".* *"The balance of epidemiologic evidence indicates that mobile phone use of less than 10 years does not pose any increased risk of brain tumor or acoustic neuroma. For longer use, data are sparse and any conclusions uncertain. From the available data, however, it does appear that there is no increased risk of brain tumor in long-term users, with the exception of acoustic neuroma for which there are some indications of an association."* *"For diseases other than cancer, very little epidemiologic data are available."* *"A particular consideration is mobile phone use by children. While no specific evidence exists, children or adolescents may be more sensitive to RF field exposure than adults…Children of today may experience a much higher cumulative exposure than previous generations. To date little or no epidemiological data in children are*

Citation	Objective/Methods	Results, Conclusions, Recommendations, Comments
		available." *"RF exposure has not been shown consistently to have an effect on self-reported symptoms (headache, fatigue, dizziness, concentration difficulties) or well-being."* *"Animal studies have not provided evidence that RF fields could induce cancer, enhance the effects of known carcinogens, or accelerate the development of transplanted tumors. The open questions include adequacy of the experimental models used and scarcity of data at high exposure levels."* *"There is no consistent indication from in vitro research that RF fields affect cells at the non-thermal exposure level."*
Horrey (2006)	**Performance costs associated with cell phone use while driving:** • Multiple databases and web resources, -2000; • Included: relevance to moderator variables: measures of driving performance (lane position; tracking ability, direct response to non-phone target); hand-held or-free; conversation vs information processing; in-vehicle vs remote conversation; simulator vs field test; common comparison of phone use (not dialing or otherwise manipulating phone while driving vs baseline condition (driving alone);	**23 experiments:** • Pooled effects show clear costs to driving performance by phone conversation; primarily to reaction time tasks; less to lane keeping/tracking; • Similar patterns for hands-free vs -held; • Some small differences road vs simulator. **Conclusions:** *"a) there are significant costs to driver reactions to external hazards with cell phone use;* *b) hands-free phones do not eliminate or substantially reduce these costs;* *c) different research methodologies or performance measures may underestimate these costs."*
Sanchez (2001)	**To combine state-of-the art research and international conclusions:** • Effects of mobile phones on environmental, individual, and population health; • CAHTA assessment; • Full text in Catalan; • English abstract does not report full methods details.	*"The scientific evidence provided by epidemiological and experimental research is incomplete, and it shows important methodological limitations, the most important being, probably, the lack of a sufficiently high number of subjects in studies with a long exposure time and an extended latency period. All authors coincide in mentioning this problem and clearly point out that the observed negative results are strictly related to short exposure to mobile phones' (MPs') radiation and latency times. The potential impact of the use of MPs on the users' and general population health is uncertain.* *"This situation probably reflects the novelty of the generalized use of this technology, and the short time available so far to observe the occurrence of effects on health."* *"Thus, the overall evidence available does not offer a clear pattern supporting the association between exposure to radiofrequency (RF) and the effects on health (cancer, reproduction or congenital defects, cognitive problems, epilepsy, suicide)."*

Citation	Objective/Methods	Results, Conclusions, Recommendations, Comments
		"There is no evidence that RF energy emitted by MPs may cause problems, but there is insufficient evidence to conclude that it poses no risk. It is impossible to state that exposure to RF radiation (even below permitted levels) has no adverse effects on population health." *"However, new evidence is being obtained (in vitro and in vivo) that some biologic effects may appear below permitted levels…variability in susceptibility and genetic predisposition…cannot be categorically asserted that RF exposure has no adverse health effects."*

Table 2: Subsequently published primary studies eligible for Table 1 reviews

Citation	Objective/Methods	Results/Conclusions
Deltour (2009)	**Time trends for incidence of glioma and meningioma:** • Denmark, Finland, Norway, and Sweden; • National cancer registries,1974-2003; • Joinpoint regression analyses.	**59,984 men and women 20-79 years diagnosed:** • Population of 16 million adults; • 1974-2003; incidence of glioma increased 0.5% per year (CI, 0.2-0.8%) among men and 0.2% (-0.1-0.5%) among women; meningioma after early 1990s 0.8% (0.4-1.3%) and 3.8% (3.2-4.4%) respectively. **Conclusions:** *"No change in incidence trends were observed from 1998-2003, the time when possible associations between mobile phone use and cancer risk would be informative for an induction period of 5-10 years."*
Schüz (2009)	See Table 3	
Shoemaker (2009)	**Case-control:** • Thames (South England) section of Interphone with minor variations; • **Cases:** Pituitary tumors in 18-59 year olds residing in area at time of diagnosis in neurosurgical center, oncology unit, or identified through registry (1 December 2000- 28 Feb 2008); • **Controls:** 1/case selected from patient lists of area GPs; • **Exposure:** any phone use < 1 year before diagnosis ignored; time of first phone use to diagnosis recorded by interview.	**506 pituitary ademonas:** • 317 (63%) participated; • 1464 eligible controls, 630 (43%) interviewed; • Cases vs controls: similar gender and age distributions but slightly higher affluence in controls; • Ever use of phone: cases, 92%; controls, 92%; • Regular use: cases, 60%; controls, 61%; • Risk of pituitary tumor not increased in regular users overall: OR, 0.9 (CI, 0.7-1.3); • > median 51 hrs of use ≥10 years prior to diagnosis: OR 1.6 (0.8-3.6); • Regular analog use: OR, 1.0 (0.6-1.6); digital, OR, 0.9 (0.7-1.3). **Conclusions:** *"We found no evidence that the risk of developing pituitary tumors is associated with cellular phone use over the induction periods and intensities of use observed."*

Table 3: Significant primary studies: INTERPHONE* and Danish cohort

Citation	Objective/ Methods	Results/Conclusions
Interphone Study		
IARC (2009)	Interphone status	Final manuscript (glioma and meningioma) by all collaborating centers (pooled results) in progress for peer-reviewed publication
Shoemaker (2009)	Table 2	
Cardis (2007)	**Interphone** **Design, methods, subjects:** • Multi-national case-control: • Does mobile phone use increase the risk of cancer in tissues most exposed (glioma, meningioma, acoustic neuroma, parotid gland tumors)? ; • Amount and direction of potential recall or participation biases? • Are RF fields from phones carcinogenic? • 13 countries: Australia; Canada; Denmark; Finland; France; Germany; Israel; Italy; New Zealand; Norway; Sweden; UK all used common core protocol • **Cases:** identified through treatment centers for diseases, usually in major metropolitan centers capturing 90-95% of cases (confirmed first diagnosis of glioma, meningioma; acoustic neuroma) • All residents 30-59 years of age in study areas; • **Controls:** randomly selected from same source population in sampling frame determined locally and individually matched (age, sex, study region) to cases; • Number of of controls to each case determined according to tumor type; • Exposure determined by self-report: regular use = at least one call per week for ≥ 6 months; type of phone (network operator ; distribution of rural vs urban use; moving vs stationary; antenna extended; duration of calls; hand-held or free); • Validation studies for exposure estimates by network operator or other data.	**Methods description only; results not yet available:** See IARC (2009), Table 2.
Hours (2007)	**French section case-control:** French with English abstract	**490 cases:** 160 glioma; 190 meningioma; 140 neuroma

	• **Cases:** residents of Paris or Lyon; 30-59 yrs; newly diagnosed with first primary glioma, meningioma, or cranial neuroma; • **Controls:** matched for age, gender, place of residence; randomly drawn from electoral rolls; • Exposure from detailed computer-assisted interview.	**639 controls** • Regular phone use: OR for glioma, 0.92 (CI, 0.53-1.59); meningioma, OR, 0.74 (CI, 0,43-1.28); • NS ORs but trend for increased risk of glioma among heaviest users (long-term, heavy use, number of phones.) **Conclusions:** *"No significant increased risk for glioma, meningioma or neuroma was observed among cell phone users participating in Interphone. The statistical power of the study was limited, however. Our results, suggesting the possibility of an increased risk among the heaviest users, therefore need to be verified in the international INTERPHONE analyses."*
Sadetzki (2007)	**Case-control** **Cell phones and risk of parotid tumors:** • **Cases:** adult Jewish Israelis with confirmed diagnosis (Jan 2001-Dec 2003) of benign or malignant parotid tumor; • **Controls:** randomly selected from national population registry and individually matched to cases (up to 7/case) for age, gender, interview date; • Analyses stratified to ipsilateral and contralateral phone use.	**402 benign, 58 malignant tumors/1266 controls:** • Ever regular phone user: OR, 0.87 (P = 0.3);no increased risk for parotid tumors in this or any other measure of exposure; • Analyses restricted to current regular users or conditions of heaviest use (e.g., rural) showed consistently elevated risks; • Ipsilateral use: highest ORs in cumulative exposure without hands-free devices (OR, 2.58; CI, 1.11-2.24; • Contralateral: OR NS. **Conclusions:** *"Our results suggest an association between phone use and parotid gland tumors."*
Danish (retrospective) cohort		
Schüz (2009)	See below; excluded from cohort because inclusion would restrict generalizeability: corporate accounts; errors in address; <18 yrs at time of first phone use; permanent resident of Faroe Is or Greenland.	**Follow up through 2003 for hospital contacts (SHRs):** • 420,095 cohort members with 4 million person-years at risk; • 10.6% had cell phone subscriptions before 1992,46.9% took subscriptions in 1995; age distribution changed with time; • Small but significant excess of hospital contacts for migraine and vertigo, smallest among long-term phone users; other SHRs close to unity; • No associations for dementia (AD, vascular, other); Parkinson's or epilepsy among men. **Conclusions:** *"The excesses of migraine and vertigo observed in this first study on cellular telephones and CNDS disease deserve further attention. An interplay of a healthy cohort effect and reversed causation bias due to prodromal syndromes impedes detection of a possible association with dementia and Parkinson disease. Identification of the factors that result in a healthy cohort might be of interest for the elucidation of the etiology of these diseases."*
Schüz (2006)	See row below	**Extended follow up (through 2002):** • 723,421 cell phone users; • 14,249 cancers observed: (SIR, 0.95; CI, 0.93-0.97) men and women combined; • Cell phone use not associated with increased risk for brain (SIR, 0.97), acoustic neuroma (0.73), salivary gland (0.77), or eye (0.96) tumors or leukemia (1.00);

		• Among subscribers of ≥ 10 yrs; no significant association with brain tumors (SIR, 0.77; CI, 0.44-0.99) and no time trend since first subscription; • Risk for smoking-related cancers decreased among men (SIR, 0.88; CI, 0.86-0.91.) but increased among women (SIR, 1.11; CI, 1.02-1.21); • Data on income and smoking prevalence among men indicated that phone use starting in mid-1980s had higher incomes and smoked less than rest of general population. **Conclusions:** *"We found no evidence for an association between tumor risk and cellular telephone use among either short-term or long-term users. Moreover, the narrow confidence intervals provide evidence that any large association of risk of cancer and cellular telephone use can be excluded."*
Johansen (2001)	**Cross-sectional:** • All Danish cell phone subscribers, 1982-1995 identified from 2 operating company lists; • Cancer cases (CNS, salivary glands) identified from national registry; • SIRs calculated.	**420,994 cell phone users:** • 3391 cancers observed, 3825 expected; • Significantly decreased SIR: 0.89 (CI, 0.86-0.92) • Substantial portion of decreased risk attributed to deficits of lung cancer and other smoking-related diseases. • No excess incidence of CNS or salivary gland tumors: SIRs 0.95 (CI, 0.81-1.12) and 0.72 (0.29-1.49), respectively and did not vary by duration of phone use, time since first subscription, age at first use, or phone type. **Conclusions:** *"The results of this investigation do not support the hypothesis of an association between cell phone use and tumors of the brain, salivary glands, or other cancers."*

*** Interphone study group results other than primary associations with personal cell phones not included.**

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