Swedish review strengthens grounds for concluding that radiation fr...nd cordless phones is a probable human carcinogen – Pathophysiology



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## groups, advise prevention in light of these concerns by taking the simple precaution of "distance" to minimize exposures to the brain and body. We note than brain cancer is the proverbial "tip of the iceberg"; the rest of the body is

Keywords:

Brain cancer, Mobile phone, Non-ionizing radiation, Microwave radiation, Epidemiology, Case–control, Misclassification, Precautionary advice, WHO, IARC, Human carcinogen, 2A, 2B, Acoustic neuroma, Acute lymphoblastic leukemia, Acute lymphocytic leukemia, Acute myelogenous leukemia lymphoid leukemia, Supply of oncologists, Health services

### 1. Background

also showing effects other than cancers.

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Chronic disease epidemiologists studying the etiology of rare diseases necessarily study people's past reported or documented exposures over decades to determine how exposure differed between those who succumbed to illness and those who did not. In so doing, epidemiologists rely on a variety of tools having both strengths and limitations.

Examining general time trends of disease and ages of diagnosis can yield hypotheses about *historical* changes in underlying causal factors, but cannot be relied on to predict *future risks*. For example, the relatively rapid growth in lung cancer in women in industrial countries in the 1970s and 1980s provided a broad and long-predicted indication of the impact of smoking. Similarly, reports in the 1980s of surges in rare ailments such as Kaposi's sarcoma in men under age 30 tied to HIV/AIDS, or rare vaginal adenocarcinoma in pre-adolescent girls whose mothers had taken the hormone diethylstibestrol early in pregnancy, have provided important clues about avoidable etiologic factors.

As a matter of public policy, societies around the world are paying the price now for having ignored earlier warnings of public health experts about the need to curtail tobacco, asbestos, vinyl chloride, DES, or to take steps to prevent HIV/AIDS transmission. The costs for treating the ravaging diseases caused by these avoidable environmental health threats have skyrocketed, while the estimated costs of strategies to prevent them pale in comparison.

# 2. Swedish analysis confirms brain cancer risks from mobile phone radiation

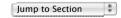
An important new article by the Swedish group of investigators led by Hardell et al. [1] provides a valuable contribution to the epidemiological literature that makes the case for creating preventive policies now to reduce harmful risks associated with mobile (cellular) and cordless phones, and other forms of wireless radiation. On May 21, 2011, a committee of 30 invited scientists from 15 different countries working on behalf of the International Agency for Research on Cancer (IARC) of the World Health Organization reviewed key studies on the topic and characterized exposure to radiofrequency radiation associated with mobile phone use as Group 2B carcinogen—i.e. possibly carcinogenic to humans [2]. This is the same category as the pesticide DDT, gasoline engine exhaust, burning coal and dry cleaning chemicals, and jet fuel—compounds that are subject to serious regulation and control around the world today.

By reviewing key epidemiological studies, some of which have been published since the IARC review, addressing methodological critiques of their own and other studies, and reporting the results of a meta-analysis of their own and the IARC coordinated Interphone study, Hardell et al. provide new and compelling evidence for IARC to re-evaluate its classification of "a possible carcinogen", with a view to changing that assessment of electromagnetic radiation from mobile phones, cordless phones, and other wireless devices at least to a "probable human carcinogen," i.e. Group 2A.

This important review concentrates on the data relating to long-term use of mobile and cordless phones from the handful of case-control studies that have been conducted on the association of mobile phone use with brain tumors, addresses arguments that have questioned the validity of past studies, extended the period of follow-up from first exposures, explains the limited nature of time-trend analyses of rare events such as brain cancer, and provides a cogent analysis of the need for precautionary steps to be taken at this time.

In their article, the Hardell group makes the controversies in this field of enquiry accessible. Being a broad-based state-ofthe-art and state-of-knowledge review, their article could serve as an excellent teaching tool in epidemiology graduate programmes. The thoroughness of their documented responses to critiques, includes re-analysis of their own and other data sets and makes possible the rejection of alleged of bias in their own studies' selection/exclusion criteria. Further, the methodological comparisons across the various studies over time, and the observation that, as the exposure period increases, so too do the risk estimates, are compelling for public health action. Finally, the way that the Group was able to integrate exposures both to cordless and mobile phone or cellphone use constructively advances this field of investigation.

# 3. Age-adjusted population trends and cohort studies of brain cancer are of limited power



As a general matter, population trends are of limited immediate value in evaluating a rare disease like brain cancer that is known to have a long latency. The survivors of the atomic bombs that fell at the end of World War II did not exhibit any increased rate of malignant cancer of the brain until four decades later. This established a long latency between exposure



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and the development of brain cancer and has important implications regarding the evaluation of environmental factors. As an editorial commentary on the release of the Interphone study noted "None of today's established carcinogens, including tobacco, could have been firmly identified as increasing risk in the first ten years or so since first exposure" [3].

Regarding cohort studies of rare events, as many have noted, the only study to approximate a cohort design of brain cancer risk over time in a population—the Danish Cohort Study—does not comport with required methods to do so [4]. In the Danish study, less than half a million registered mobile phone users were followed and the authors concluded that there is no increased risk. In this study, no direct information on cellphone use was available. Further, the rapidly changing nature of exposure to microwave radiation from cellphones, cordless phones and other similar sources of exposure was not considered. In addition, corporate users, people who would have been the heaviest users, were included in the unexposed group. Corporate users, amounted to almost a quarter of a million people in the 1990s and are known to have used these technologies four times more often than those in this study. Finally, updates to this cohort also lost significant numbers of the original group to follow-up [[5], [6]]. As a result, it is impossible to take the reported study results of no increased risk at face value, especially considering that a cellphone "user," as defined by the Interphone study, was anyone who made one call a week for 6 months.

### 4. Case–control studies are powerful for studying Jump to Section : mobile phone radiation

In general, epidemiologists appreciate that, for the study of rare diseases, such as brain cancer, the case–control design is far more powerful than a cohort study. In fact, all of the few well-designed case–control studies of this issue have found significantly increased risk after a decade of use, with higher risks occurring in those with highest use. Thus, within Interphone Appendix II, those who used phones for 1640 h or more had close to a doubled risk of glioma.

As a number of commentators and several of the principal investigators of the Interphone studies have noted, the Interphone study results are limited in many ways [[7], [8]]. The Interphone study did not include information on exposure to cordless phones or other wireless devices, did not include patients who began using these technologies before age 20, and included no cases that occurred after 2005 [[9], [10]].

As a result, the Interphone results likely underestimate current risks from mobile phones, and cannot be relied on to shed light on the risks for those who began using phones as children or teenagers. Adults and children now use cellphones for many hours a day compared to only 2–2.5 h a month at the time the Interphone study was conducted.

Further, any study that categorizes people who used cordless or portable phones (which emit the same microwave radiation as cellphones) as 'unexposed,' increases the chances of finding no effect when a real one may well be present. This is because the study is comparing people who were actually 'exposed' with others who are considered to have been unexposed, but were, in fact, also 'exposed' to radiofrequency fields. Because the Nordic countries were early users of mobile phones, it was possible for the Hardell group to conduct case–control studies on those who began using cellphones and cordless phones before age 20. So far, they are the only group in the world that has investigated an increased risk from long term usage that began in those under age 20. Consistent with the increased sensitivity of the young to toxic agents, the highest risk of tumors occurred for those who began using wireless phones as teenagers, or earlier, with glioma risk increased fourfold (OR 4.3, 95% CI = 1.2–5.5), and acoustic neuroma risk increased almost sevenfold (OR 6.8, 95% CI = 1.4–34) for ipsilateral use.

An especially important result of the latest Hardell analysis is the finding that patient survival is reduced where mobile phone use began at younger ages. "When adjustment was made for age, the cases with glioblastoma who had used wireless phones had an elevated risk of shortened survival compared to unexposed cases in our study." In addition, "a poorer survival among children with acute lymphoblastic leukemia exposed to ELF-EMF has been reported..." [1].

Other findings are consistent with an increased risk for cancers of the blood or bone marrow tied with mobile phone use. One study in Thailand found a threefold risk of leukemia from GSM cell phone use (OR 3.0, 95% Cl: 1.4–6.8) and more than a fourfold risk for any lymphoid leukemia (OR 4.5, 95% Cl: 1.3–15) [11]. Cooke et al. (2010) also reported increased Acute Lymphocytic Leukemia (ALL) and Acute Myelogenous Lekeumia (AML) risk with >15 years since first use of mobile phones, respectively OR = 1.41 (Cl = 0.45–4.37) and OR = 2.08 (Cl = 0.98–4.39, calculated *p*-value = 0.051) [12].

# 5. Exposure misclassification biases toward the null hypothesis

A Swiss personal monitoring study found that mobile phone use currently accounts for one-third of total exposures to wireless and microwave radiation, with routers and base stations accounting for the rest [13]. Misclassification of exposure is well known to bias toward the null hypothesis, or to a finding of "no effect" when, in fact, an effect may well be present. None of the studies carried out on cell phones thus far, including those of Hardell, has taken into account these important other exposures, many of which have changed quite recently and continue to rapidly expand.

Current standards rest on the assumption that permitted levels of microwave radiation from mobile phones do not induce any measureable change in temperature or biological effect. Several independent avenues of research have shown this assumption to be incorrect.

One important study from Sloan Kettering scientist, David Gultekin, and Lothar Moellaer from Cornell [14], found that

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currently used cellphones can produce hotspots in living brain tissue. Using Positron Emission Tomography (PET), the Director of the National Institute of Drug Abuse, Nora Volkow, reported that 50 min of use of a mobile phone produces significant change in glucose metabolism in the area of the brain that absorbs the most radiation [15]. Reviewing many other relevant studies on EMF impacts on the brain, Corle et al. (2012), concluded:

"A variety of human, rodent and cell culture experimental studies though inconclusive, do collectively suggest that mammalian brain tissue may be sensitive to cellphone levels of EMF" [16].

#### 6. Increased susceptibility in young people

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The dielectric properties of tissues indicate how easily material can absorb microwave radiation and determine the tissue's response to an electromagnetic current. The measured properties are the conductivity ( $\sigma$ ) – which is directly proportional to the SAR, and the permittivity ( $\varepsilon$ ). Empirical data have shown a difference in the dielectric properties of tissues as a function of age. These differences are mostly due to the higher water content in children's tissues, but they also reflect the physiological development of an organism or tissue that involves structural and biochemical changes. The results of studies on age effects showed that, while the dielectric properties of gray matter do not change with age, other tissues such as white matter and spinal cord vary significantly. More significant results were observed in the case of bone, skull and marrow tissues [[17], [18], [19], [20]].

High resolution computerized models based on real human imaging data suggest that the higher conductivity and higher permittivity in children's brain tissues, together with their thinner skulls and smaller heads, will lead to higher SARs in their brains from microwave frequencies when compared to adults. Exposure to other body organs from cellphones carried in the pockets is common. Effects on other body organs are studied as well as in utero effects on the fetus [[21], [22], [23], [24], [25], [26], [27], [28], [29]].

These and many other studies provide important evidence that biological effects from mobile phone radiation occur with contemporary phones and thus strengthen the case for expecting these devices to have impacts on health.

A letter to the U.S. Congress by the American Academy of Pediatrics, dated 12 December 2012 notes:

"Children are disproportionately affected by environmental exposures, including cell phone radiation. The differences in bone density and the amount of fluid in a child's brain compared to an adult's brain could allow children to absorb greater quantities of RF energy deeper into their brains than adults. It is essential that any new standards for cell phones or other wireless devices be based on protecting the youngest and most vulnerable populations to ensure they are safeguarded through their lifetimes."

#### 7. Shortage in oncology services

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Projected supply for oncology services in the U.S. is not expected to meet demand in the near future and is already inadequate. In 2007 a study for the American Society of Clinical Oncology (ASCO, 2007) [projected that "supply is projected to only increase 20% between now and 2020, and capacity for oncologist visits is projected to rise even less at 14%. Demand for oncologist services is projected to grow by 48% during that same time" [30]. The projections were based on current cancer rates and delivery patterns applied to the expected U.S. population in 2020. Unless there is a dramatic change in cancer care treatment or delivery between now and 2020, the nation is expected to face an acute shortage of oncologists." Thus, the number of available oncologists is about half those projected to be needed by 2020.

If the elevated risks found in studies of young cellphone users were to occur globally, then rates of glioma could rise significantly from about 3 to 12 per 100,000. In addition to the direct medical costs involved, there will be substantial indirect costs for society, including loss of productivity of those at the peak of their professional lives and incalculable family impacts. This could create a devastating impact on the capacity to deliver neuro-oncology services.

### 8. Policy implications and research priorities

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A new question that these findings raise is profound: could mobile phone radiation not only cause brain cancers, but could its continued use shorten the lives of those who develop these and other diseases? This prospect raised by the analysis of Hardell et al. should be sufficiently concerning to prompt health authorities around the world to issue advice, especially to their incident cancer patients, to reduce exposures from mobile and cordless phones, while further work continues to explore this matter.

Other important research questions that should be addressed include the following: Could exposures to mobile phone radiation play a role in the unusual rise in autism? Does the increase in deep vein thrombosis as the leading cause of death in pregnancy have any connection with the growing use of mobile phones during pregnancy? Could blood clots such as that developed by Secretary of State Hillary Clinton after a fall be more frequent in those who are also heavy cellphone users? Are tinnitus and other hearing problems associated with longer-term mobile phone use?

About half of the world's mobile phone users are under age 30 today and live in developing countries. If the risks reported by Hardell et al. were to occur in that population, the capacity to provide health care would be overwhelmed. This year, the Central Brain Tumor Registry of the United States (CBTRUS) estimates that in the U.S. about 10,000 people will develop glioma. CBTRUS reports that gliomas constitute 1 of every 3 brain tumors and 4 out of every 5 malignant brain tumors. If current young users of mobile phones face such heavy risks, then several thousand new cases will develop in the U.S. annually. Oncology surgeons, neuro-oncologists, drugs and nurses are already in short supply in many regions of both the

developed and developing world. Prognosis for the disease has not changed appreciably, with five-year survival rates being about 5% (CBTRUS, 2012) [31].

Current standards for exposure to radiofrequency fields were set more than fifteen years ago resting on the belief that levels of microwave radiation from mobile phones cannot induce any measureable change in temperature or other biological effect. Recent analyses show that this assumption is no longer tenable. The General Accountability Office (GAO) recently advised the U.S. Congress that standards for mobile phones should be reassessed (GAO, 2012), noting that no new proposals had been advanced in the past two decades, a period during which both the users and their uses have changed dramatically.

In considering the overall findings on increased risk of brain cancer and mobile phone and other wireless radiation in its 2011 evaluation, IARC Director, Christopher Wild, offered some simple recommendations that have since been widely shared:

"Given the potential consequences for public health of this classification and findings it is important that additional research be conducted into the long-term, heavy use of mobile phones. Pending the availability of such information, it is important to take pragmatic measures to reduce exposure, such as hands-free devices or texting" [32].

## 9. Liability, simple precautions, and product

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#### warnings

Over the past decade, this advice about reducing exposures through simple precautions has been echoed by a growing number of health professionals and regulatory bodies around the world, including the Finnish Radiation and Nuclear Safety Authority, the Health Safety Authority of Britain, the Israeli Health Ministry, the Indian government's Department of Telecom, the Austrian Medical Society, the American Academy of Pediatrics, Environmental Health Trust, Environmental Working Groups, and many others.

With 5.9 billion reported users worldwide, mobile phones constitute a new, ubiquitous and rapidly growing environmental exposure. In 2011, following publication of the Interphone study results, two of the Interphone study researchers including lead author Cardis published an editorial on the potential public health implications of possible brain tumor risk in mobile phone studies [33]. The authors expressed their concern that small increases in risk, especially those found in ipsilateral localized exposure and in long term users are important when considering the huge numbers of people exposed:

"...The findings in several studies of an increased risk for glioma among the highest users on the side of the head where the phone was used and, in Interphone, in the temporal lobe are therefore important. These are the findings that would be expected if there was a risk, as these are the a priori relevant exposure variables."

"Even a small risk at the individual level could eventually result in a considerable number of tumours and become an important public health issue. Simple and low-cost measures, such as the use of text messages, hands-free kits, and/or the loud-speaker mode of the phone could substantially reduce exposure to the brain from mobile phones."

Saracci and Samet's commentary (2010), while less unequivocal, supports this view [3]. Since the risk of greatest interest is lifelong use, possibly beginning in childhood—a pattern of exposure that cannot yet be studied, the authors agree that a precautionary approach to the extent and manner of use of mobile phones may find some support in the elevated risks noted in subjects with the highest exposures.

There are a number of experts who contend that the lack of an overall positive trend in gliomas provides evidence that mobile phone use does not cause brain tumors [[34], [35], [36]]. In addition, some assert that there is no exposure– response relationship, either in terms of the amount of mobile phone use or by localization of the brain tumor, and that this argues against a causal association [37]. But, reviews conducted by groups of researchers from different countries, as well as published policy resolutions and advisories from national authorities such as the Finnish Radiation and Nuclear Safety Authority and the Austrian Medical Society, reach much different conclusions and fully support the need for a precautionary approach regarding risk.

The grounds for taking precautionary steps rest on a growing body of evidence.

Abdus-salam et al., 2008: "the need for caution is emphasized as it may take up to four decades for carcinogenesis to become fully apparent" [38].

Myung et al., 2009: "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" [39].

Levis et al., 2011: "Our analysis of the literature studies and of the results from meta-analyses of the significant data alone shows an almost doubling of the risk of head tumors induced by long-term mobile phone use or latency" [40].

Committee on the Environment, Agriculture and Local and Regional Affairs of the Council of Europe (2011): "[For mobile phones] One must respect the precautionary principle and revise the current threshold values; waiting for high levels of scientific and clinical proof can lead to very high health and economic costs, as was the case in the past with asbestos, leaded petrol and tobacco" [41].

The Russian National Committee On Nonionizing Radiation Protection (RNCNIRP) "Urgent measures must be taken

because of the inability of children to recognize the harm from the mobile phone use and that a mobile phone itself can be considered as an uncontrolled source of harmful exposure" [42].

As a sign of the times, manufacturers and businesses are developing ways to promote reductions in radiation as well. One of the fastest growing mobile apps is called tawkon—which provides an algorithm indicating the potential danger from signal strength to those using phones. Globally, sales of cases and headsets tested and confirmed to reduce radiation have grown, indicating market demand for such devices.

Phone manufacturers are also issuing advice on reducing exposure, as these notices from Apple and Samsung indicate:

"To reduce exposure to RF energy, use a hands-free option, such as the built-in speakerphone, the supplied headphones, or other similar accessories. Carry iPhone at least 10 mm away from your body to ensure exposure levels remain at or below the as-tested levels. Cases with metal parts may change the RF performance of the device, including its compliance with RF exposure guidelines, in a manner that has not been testified or certified."

What is missing altogether in the above statement is this previously published advice from Apple that these phones, when carried in the pocket, can exceed the FCC exposure guidelines.

Warning: "iPhone's SAR measurement

may exceed the FCC exposure guidelines

for body-worn operation if positioned less

than 15 mm (5/8 inch) from the body (e.g,

when carrying iPhone in your pocket)."

Such advice about safer use no longer appears in a printed pamphlet with iPhones, but can be found on the phones by clicking settings/general/about/legal/RFexposure.

Other manufacturers also include more safety advice. Samsung is the number one producer of cellphones in the world today. Their new Convoy 2 phone comes with this advice:

"Your mobile device is not a toy. Do not allow children to play with it because they could hurt themselves and others, damage the device, or make calls that increase your mobile device bill."

"Keep the mobile device and all its parts and accessories out of the reach of small children."

The challenge to public health is how to promote sensible policies now. The focus on brain cancer may be the tip of the iceberg in relation to a host of other serious widespread health, behavioral and social effects from such radiation. Downloadable resources that draw upon advisories developed by experts in many nations are available in several languages at <u>www.ehtrust.org</u>.

#### 10. Practical advice for the public

When it comes to using electronic devices, remember: Distance is your friend.

- Don't hold a cellphone directly up to your head. Use a headset or speakerphone when using the device, or a non-metal case that has been independently tested to reduce radiation up to 90%.
- Pregnant women should keep cellphones away from their abdomen and men who wish to become fathers should not keep these phones on while in their pocket.
- Don't allow children to play with or use your cellphone. Older children should use a headset or speakerphone when talking on a cellphone.
- Do not text and drive and only use specially adapted antennas when using mobile phones in cars to avoid absorbing maximum power as the phone moves from one cell system to another. When buying a new car, pay attention that the car has a built-in antenna that reduces your direct exposure.
- Turn off your wireless router at night to minimize exposure to radiation.
- Eat green vegetables and get a good night's sleep in a dark room to enhance natural repair of DNA that may have been damaged by radiation.

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