

Report

CSAT

Swedish Council for
Working Life and
Social Research

Research during the last ten years

RADIOFREQUENCY ELECTROMAGNETIC FIELDS

– Risk of disease and ill health

RADIOFREQUENCY ELECTROMAGNETIC FIELDS AND RISK OF DISEASE AND ILL HEALTH

– Research during the last ten years

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Foreword

The Swedish Council for Working Life and Social Research (FAS) was commissioned by the Government to monitor issues relating to research into electromagnetic hypersensitivity and to document and report on the state of research at regular intervals, starting in 2003.

In order to carry out its mandate, FAS assigned Professor Anders Ahlbom of the Institute of Environmental Medicine at Karolinska Institutet to work with a project group to produce annual reports on scientific developments in the field. The group has consisted of Professor Maria Feychting, Professor Yngve Hamnerius, Associate Professor Lena Hillert, and Professor Anders Ahlbom (chair). The group presented its first report in 2003 and has since then published annual reports through 2010.

The Government's mandate read as follows:

“FAS is to monitor research into electromagnetic hypersensitivity. Under this mandate the Council is to work with other research bodies, authorities and parties that FAS deems appropriate to document and provide information on the state of research every other year.”

This special mandate from the Ministry of Health and Social Affairs came to an end at the beginning of 2012. FAS then tasked Professor Ahlbom with producing a summary of the previous reports. This report follows.

Because almost ten years have elapsed since the first report was published, the group has been asked to look back at the previous decade to see how the state of knowledge has developed over that period. Electromagnetic fields are encountered in many situations and their characteristics with respect to strength, frequency, and modulation vary depending on origin and usage. However, the vast majority of research during the last decade addresses the type of electromagnetic fields that are used in connection with mobile communication, often referred to as radiofrequency fields. Possible health risks related to exposure to those fields are the focus of this review.

Stockholm, June 2012

Erland Hjelmquist
Secretary-General
Swedish Council for Working Life and Social Research

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Executive Summary

The focus of this report is electromagnetic fields of the type that occur in connection with mobile telephony, so called radio frequency (RF) fields and the possibility that exposure to such fields poses a risk of disease or ill health. The purpose is to describe what was known ten years ago, what we have learned during the past decade, and where we stand today.

TEN YEARS AGO

The mechanism of interaction between RF fields and the human body was established long ago and is increased temperature of exposed tissue (compare microwave ovens). Methods for measurements of the fields in the air were developed early but the data on distribution of the absorbed energy in the human body was still restricted. Data regarding sources and levels of exposure to the population was limited because systematic measurements had not been conducted. A considerable number of provocation studies on exposure to fields of lower frequencies (related to electric power and computer screens) had already been conducted and had not found any evidence of an association to symptoms (headache, vertigo, dizziness, concentration difficulties, insomnia) but the corresponding information about RF fields and occurrence of symptoms was scarce. Few and methodologically limited epidemiological studies had been conducted on RF field exposure and cancer.

WHAT WAS LEARNED DURING THE PAST TEN YEARS

Extensive research on various aspects of RF fields has been conducted during the last ten years and the knowledge

database has increased considerably. Simulation models have improved our knowledge about how the fields and the energy are distributed in the body. Mobile, so called, exposimeters have been developed for use in epidemiological studies. Many more measurements have been conducted to increase our knowledge about sources and level of exposure to the population.

More than 15 provocation studies (single or double blind) have been conducted on symptoms attributed to exposure to RF fields. These studies have not been able to demonstrate that people experience symptoms or sensations more often when the fields are turned on than when they are turned off. One longitudinal study has looked at frequency of symptoms in relation to environmental exposure and this study found no association between exposure and symptoms.

A considerable number of studies on cancer, and in particular brain tumor, were presented. As a consequence there exist now very useful data including methodological results that can be used in the interpretation of this research. With a small number of exceptions the available results are all negative and taken together with new methodological understandings the overall interpretation is that these do not provide support for an association between mobile telephony and brain tumor risk. In addition, national cancer statistics are very useful sources of information because mobile phone usage has increased so quickly. Had mobile phone use and brain cancer risk been associated it would have been visible as an increasing trend in national cancer statistics. But brain cancer rates are not increasing.

WHERE WE STAND TODAY

We now know much more about measurements and absorption of RF fields and also about sources of exposure to the population and levels of exposure. A considerable number of provocation studies on RF exposure and

symptoms have been unable to show any association. Overall, the data on brain tumor and mobile telephony do not support an effect of mobile phone use on tumor risk, in particular when taken together with national cancer trend statistics throughout the world.

Research on mobile telephony and health started without a biologically or epidemiologically based hypothesis about possible health risks. Instead the inducement was an unspecific concern related to a new and rapidly spreading technology. Extensive research for more than a decade has not detected anything new regarding interaction mechanisms between radiofrequency fields and the human body and has found no evidence for health risks below current exposure guidelines. While absolute certainty can never be achieved, nothing has appeared to suggest that the since long established interaction mechanism of heating would not suffice as basis for health protection.

Sammanfattning

Denna rapport är inriktad mot det slags elektromagnetiska fält som förekommer i samband med mobiltelefoni, så kallade radiofrekventa fält (RF) och möjligheten att exponering för sådana fält innebär en risk för sjukdom eller ohälsa. Syftet är att redovisa vad som var känt för tio år sedan, vad som har framkommit under det senaste decenniet och var kunskapen står i dag.

FÖR TIO ÅR SEDAN

Mekanismen för interaktion mellan RF-fält och människa har varit känd sedan länge och består i att temperaturen i exponerad vävnad ökar (jmf mikrovågsugnar). Metoder för att mäta fält i luft utvecklades tidigt men kunskapen om hur den överförda energin fördelades i kroppen var fortfarande begränsad. Informationen om källor och nivåer av exponering till befolkningen var ofullständig därför att systematiska mätningar inte hade genomförts. Ett betydande antal provokationsstudier av fält med lägre frekvens (kopplade till elanvändning och bildskärmar) hade redan genomförts, dock utan att finna något stöd för ett samband med symtomförekomst (huvudvärk, svindel, yrsel, koncentrationssvårigheter, sömnbesvär) men det fanns fortfarande mycket lite information av detta slag för RF. Få och metodologiskt utvecklade epidemiologiska undersökningar hade genomförts på RF-exponering och cancer.

VAD HAR FRAMKOMMIT UNDER DET SENASTE DECENNIET

Omfattande forskning på skilda aspekter av RF-fält har utförts under de senaste tio åren och kunskapsdatabasen har utökats avsevärt. Simuleringsmodeller har förbättrat kunskapen om hur fälten och energin fördelas i kroppen.

Mobila, så kallade exposimeters, har utvecklats för användning i epidemiologiska undersökningar. Ett stort antal mätningar av RF-fält har genomförts och kunskapen om exponeringskällor och exponeringsnivåer i befolkningen förbättrats.

Åtminstone 15 provokationsstudier (enkel- eller dubbelblinda) har gjorts på symtom som attribuerats till RF-exponering. De studierna har inte kunnat visa att personer upplever symtom eller känner av fält mer ofta när fälten är påslagna jämfört med när de är avslagna. En longitudinell studie har undersökt symtom i relation till exponering i miljön utan att finna något samband.

Ett betydande antal epidemiologiska undersökningar av tumörer, och särskilt hjärntumörer, har redovisats. Dessa har också tillfört värdefull metodologisk information som kan utnyttjas vid tolkning av undersökningsresultat. Med några få undantag är dessa undersökningar negativa och med beaktande av den nya metodologiska kunskapen är den samlade bedömningen att dessa undersökningar inte ger stöd för ett samband mellan mobiltelefoni och hjärntumörrisk. Nationell cancerstatistik tillför också mycket användbar information därför att mobiltelefonanvändningen har ökat så snabbt. Om mobiltelefoni hade varit kopplat till en ökad hjärntumörisk hade detta framkommit som en ökande trend i nationell cancerstatistik. Men hjärntumörsjukligheten ökar inte.

SITUATIONEN I DAG

Kunskapen om mätningar och upptag av RF-fält i kroppen liksom om källor till exponering och exponeringsnivåer i befolkningen har utökats i mycket hög grad. Ett betydande antal provokationsstudier har gjorts, dock utan att kunna påvisa ett samband mellan exponering och symtomförekomst. De data som nu finns om mobiltelefoni och hjärntumörisk tyder inte på att det finns ett samband,

särskilt inte i beaktande av nationella cancertrender runt om i världen.

Forskning om mobiltelefoni och hälsa startade utan att det fanns en biologiskt eller epidemiologiskt grundad hypotes om möjliga hälsorisker. Motivet var i stället en allmän oro för en ny teknik som spreds mycket snabbt över världen. Omfattande forskning under mer än ett decennium har inte påvisat något nytt avseende interaktion mellan RF-fält och människa och har inte heller funnit stöd för att det skulle finnas hälsorisker vid exponering på nivåer under aktuella gränsvärden. Även om fullständig säkerhet aldrig kan erhållas så har det hittills inte framkommit något som tyder på att den sedan länge etablerade mekanismen om temperaturstegring inte skulle vara en tillräcklig grund för riskvärdering.

Introduction

At the center of this report are electromagnetic fields belonging to the lower end of the electromagnetic spectrum. They have too low energy to break chemical bonds, including the bonds in macromolecules such as DNA. Thus, they cannot create ions and belong therefore to the part of the electromagnetic spectrum that is referred to as non-ionizing radiation.

While such electromagnetic fields occur in connection with an increasing number of different technologies and usages the dominating sources are production, distribution, and use of electric power (extremely low frequency fields, ELF) and mobile telecommunication (radiofrequency fields, RF).

The mechanisms of interaction between the fields and the human body were established long ago. In case of fields generated in connection with electric power distribution and usage the interaction mechanism is via induced currents and nerve and muscle stimulation and in case of fields used for mobile communication the interaction mechanism is increased movement of water molecules and as a consequence increased temperature of exposed tissue (compare microwave ovens). These effects are transient. Currently existing exposure guidelines are formulated in order to protect against health effects from these interactions.

Established mechanisms are not consistent with the concept that exposure to ELF and RF fields would have any health effects in humans below current exposure guidelines. Nevertheless, reports of such effects had occurred already long time ago. Some of these early reports are the result of rather general health surveillances of

occupational populations. One example is reports from the 60's about ill health in workers in power stations in the Soviet Union. It was speculated that the effects were mediated through electric shocks rather than being a direct consequence of electromagnetic field exposure. However, the findings were never confirmed. Swedish censuses, including data on job title and industry were linked to the cancer registry and to the cause of death registry during the 70's and the 80's. This created an opportunity for epidemiological investigations to link occupations to cancer and other outcomes and this gave rise to a large number of studies and results, including data on cancer risk in occupations that might be associated with exposure to electromagnetic fields. Whenever raised risks were observed attempts were made to design more pointed research in order to confirm or falsify the observation. Similar research was also done in other countries and included for example several studies on military occupations, including radar operators. However, the exposure information was notoriously too crude for these studies to provide valuable information in the context of electromagnetic fields and health risks and none of the observed raised risks could be confirmed in follow up research.

Other lines of research started out from concerns that use of certain equipment might imply exposure to electromagnetic fields and that health risks might follow as a consequence. One example is work with computer screens. This became an active research area when computers were relatively new in the work place and employees became worried. A wide range of health problems, spanning from negative pregnancy outcome to skin irritation, were implicated. Despite intense research efforts it was never established that electromagnetic field exposure during work with computer screens was associated with any health problems. However, the issue was resolved rather pragmatically by a gradual shift in technology towards screens with lower emissions and

finally by the abandon of cathode ray tube screens in favor of LCD screens.

An area that has attracted considerable attention is “electromagnetic hypersensitivity”. It refers to the concept that exposure to electromagnetic fields would lead to the development of a sensitivity in some individuals that would imply that various symptoms and sensations occur as a consequence of electromagnetic field exposure. Alternatively, “electromagnetic hypersensitivity” could mean that a part of the population is particularly sensitive, for reasons unrelated to electromagnetic fields, but that they still experience symptoms and sensations when exposed to such fields. The implicated symptoms are rather general and include e.g. fatigue, concentration difficulties, vertigo, and headache. Symptoms following exposure to electromagnetic field exposure have been implicated in connection with work on computer screens, residency or being near sources of ELF magnetic fields such as power lines, and exposure to RF fields from mobile phones and base stations.

One topic differs from the others in this area and that is leukemia in children and exposure to magnetic fields from power lines and use of electricity. This area differs in the sense that an initial epidemiological observation about a raised risk was confirmed by later studies. A total of about a dozen later studies found more or less the same result as the initial study. This was also confirmed in several pooled and meta-analyses. This triggered extensive research also on adults and on health outcomes other than leukemia and cancer. While raised risks were observed initially in several of these lines of research, leukemia in children remained the only result that could be reasonably confirmed. Extensive experimental research aimed at trying to find an explanation to the epidemiological findings was not successful and to date there is not even a credible hypothesis for how exposure to ELF magnetic fields might play a role in the origin of leukemia.

Over time, the focus of the research on electromagnetic fields and health has varied across frequencies and techniques and also across health outcomes as indicated above. General screening of occupational groups is not done in the same way anymore and concerns about computer screens are virtually gone. Some research does continue on ELF fields generated in connection with distribution or use of electricity, but the volume is small and has been so for some time. Instead the focus has lately been on the RF fields that are used in connection with mobile communication. The health effects that have been looked upon have ranged from cancer to the type of general symptoms that are linked to “electrical hypersensitivity”. No specific biological hypothesis lies behind this research. Nor has the research been triggered by a specific observation, as was the case with the power frequency fields and childhood leukemia. Instead there was a concern that if some basic information regarding these fields or their interaction with human physiology had been missed or misinterpreted it could have huge public health consequences because mobile telephony was a new technology that spread very rapidly worldwide. This led to an intense search for possible health risks and for a deeper understanding of the interaction between RF fields and physiology.

The purpose of this report is to review how the knowledge about possible health risks associated with exposure to RF fields has evolved during the last decade. Ten years ago this was a relatively new field and information about sources of exposure, research methodology, and health effects were limited. During the last ten years quite extensive research has been conducted and information has accumulated. This leads up to what we know today. Thus, this report will describe the knowledge base ten years ago, what has been achieved since then, and where we stand today. The review is basically restricted to cancer and symptoms because these are the only outcomes with a big enough database for any conclusions to be drawn.

Radio Frequency Exposure

Everyday exposure has changed due to the introduction and spread of new mobile phone and broadcasting systems. The first public mobile phone system (NMT Nordic Mobile Telephony) was introduced in 1981 in Sweden, and the first handheld mobile phone became available 1987. After a relatively slow start, mobile phone use increased with the introduction of the GSM system in 1992. Ten years ago 87% of the Swedish population were using a mobile phone; this has increased to 97% in 2011. In 2002 only 3% of the population did not use a wired telephone, this proportion has increased to 22% in 2011. In 2002 69% of the households had access to the Internet at home, and this had increased to 91% in 2011 (Post- och Telestyrelsen, 2011). In year 2011, 33% of the Internet users used mobile broadband, which connects the computer to Internet via the mobile phone system. An increasing proportion of those who are using a wired Internet access uses wireless LAN. This means that we are exposed to an increasing number of radio frequency transmitters.

WHAT DID WE KNOW 10 YEARS AGO?

A measure of exposure is essential when studying biological effects of RF fields and also when assessing compliance with exposure guidelines.

A commonly used measure of the exposure is the electric and magnetic field strength in air. However, this does not give the whole picture, as the absorbed energy in the body is strongly dependent on the frequency of the fields, and the size and orientation of the body. In the seventies the concept of Specific Absorption Rate (SAR) in the body was introduced. SAR is a measure of the absorbed RF energy in the body per time and mass unit; it is given in W/kg. SAR could be calculated for simple geometrical bodies such as ellipsoids. In the eighties the data on radiofrequency absorption were put together in the Radiofrequency radiation dosimetry handbook (Durney et al., 1986). This knowledge was used when designing research on biological effects of RF fields and when

new safety guidelines were developed. Ten years ago the knowledge of the distribution of individual RF exposure in the population was very limited; the few environmental measurements that existed were mainly done close to transmitters to assess compliance with guidelines.

WHAT HAVE WE LEARNED DURING THE LAST 10 YEARS?

Dosimetry

Looking back at the last 10-year period, the most important change is in dosimetry, where advances in man models and simulation tools have revolutionized this research area. Radio frequency dosimetry describes how the external fields are absorbed in the body and how this absorption is distributed in the different organs. For RF exposure a thermal effect is the established mechanism of biological and health effects. The ICNIRP (1998) guideline, which is the basis for the EU recommendation for limiting the exposure of the general public, is based on thermal effects (ICNIRP, 1998). An elevation of temperature is closely related to the energy absorption rate (SAR) in the body during a certain time period.

RF guidelines limit the SAR levels in the body. The SAR levels are called the basic restriction, as they are related to the established mechanism, heating. The SAR levels can, however, not be directly measured in a human body. Therefore reference levels have also been introduced, which are expressed in quantities, such as the electric and magnetic field strength in the air. The reference levels have been determined so that the basic restrictions shall not be exceeded.

If a person is exposed to a whole body SAR of 4 W/kg during 30 minutes, the body temperature will increase approximately 1 °C. ICNIRP (1998) chose a whole-body average SAR of 0.4W/kg as the basic restriction for occupational exposure. An additional safety factor of 5 was

introduced for exposure of the public, giving an average whole-body SAR limit of 0.08 W/kg.

A modern mobile phone has a maximum output power of 0.25 W. Even if all transmitted power from the phone was absorbed in the head, the whole body SAR could not exceed the basic restriction. A source put in contact with the body can, however, give rise to a local heating. To protect for this, ICNIRP has also guidelines for localized exposure, where the SAR value in 10 grams of tissue is restricted. For the general public the local SAR value is limited to 2 W/kg, this limit applies to mobile phones.

Recent advances in MRI (Magnetic Resonance Imaging) have made it possible to make detailed anatomical human-body models. The human body model can be divided into small voxels. A voxel is a small volume element or cube. A whole-body human voxel model can consist of several million voxels. Each voxel is given appropriate dielectric properties according to which organ it belongs.

Voxel models of whole-body humans in various postures and of children, foetuses, and embryos have been developed; see for example (Christ et al., 2010; Dimbylow et al., 2008).

The advances in computer simulations using voxel models have made it possible to calculate the SAR distribution in the body even within different organs (Lin, 2007). Some studies (Conil et al., 2008; Dimbylow and Bolch, 2007; Kuhn et al., 2009; Nagaoka et al., 2008; Wang et al., 2006) have shown that RF exposure at the ICNIRP reference level, of bodies shorter than 1.3 m in height (corresponding approximately to children aged 8 years or younger) can give SAR levels up to 40% higher than the current basic restriction, under certain conditions and frequencies. This is, however, small in relation to the safety factors that are used.

Measurements

There have been developments of measurement instruments for measuring RF exposure during the last 10 years, although the measurement principles used have been known for a longer time. Most exposure measurements are done at a distance from the source, which is longer than the wave length (10 – 30 cm), in which cases conventional antennas can be used to measure the field strength in air. From the field strength the intensity of the exposure can be calculated and expressed in for example $\mu\text{W}/\text{m}^2$.

Instruments to measure field strength in air can be divided into broadband instruments and frequency selective instruments. If the frequencies are unknown, frequency selective instruments, such as spectrum analyzers should be used. During the last years it has been possible to reduce the size and weight of spectrum analyzers and make them

battery operated, which makes them more usable for outdoor exposure assessment.

There is an interest in epidemiologic studies to measure the personal exposure (Neubauer et al., 2007). For this purpose body worn so called exposimeters, which logs the exposure in several frequency bands, have been developed (Lehmann et al., 2006). However, also exposimeters have limitations. As the exposimeters are worn on the body, the absorbed power in the head from the person's own phone use cannot be measured. The body can also shield the radiation in some directions. Exposimeters have already been used in several studies (Bolte et al., 2008; Joseph et al., 2010; Roosli et al., 2008; Viel et al., 2009). Exposimeters makes it possible to get exposure data over time, for example 24 h measurements. Breckenkamp and colleagues measured the total exposure to radiofrequency electromagnetic fields in 1348 bedrooms in Germany (Breckenkamp et al., 2012). All measured values were orders of magnitude below the ICNIRP guidelines. Major sources of exposure were cordless phones (DECT standard), wireless LAN, and blue tooth contributing together about 82% of total exposure.

For sources that are used close to the body, such as mobile phones, external reference values cannot be used and therefore the SAR-value in the body has to be assessed. Measurements in a living human body are not possible, so measurements on phantoms are used instead. A head phantom shell is filled with a fluid that has dielectric properties like the brain. The mobile phone (or another source such as WLAN) is positioned at the outside of the phantom shell and a small measurement antenna is positioned inside the phantom. The electric field strength is measured at different positions inside the head and the distribution of SAR can be calculated from these measurements, (Okano and Shimoji, 2012; Schmid et al., 1996).

RF exposure sources

The sources that we are exposed to have changed considerably during the last decade. The first generation mobile phone system, NMT, which was introduced in Sweden 1981, was terminated 2007. The first mobile units had a transmitter unit and separate handset (so called "bag-phones"), and the output power from this unit could be up to 14 W. In 1987 portable phones with the transmitter and handset in the same unit were introduced. The output power of these units was 1 W.

The second generation of the mobile phones, GSM 900, was introduced 1992 with a peak output power of 2 W. GSM uses time domain multiple access, TDMA, which means that a phone just transmits during one out of eight time slots, which reduces the maximum average power to 0.25 W. In 1997 GSM 1800 was introduced, where the

peak output power was reduced to 1 W. These systems are currently in use.

In 2003 the third generation mobile phone system, UMTS, was introduced. The maximum output power from the UMTS phones currently in use is 0.25 W. The fourth generation mobile phone system, LTE, was introduced in 2009, with a maximum output power of 0.20 W. When this system was introduced it was only available for mobile broadband units, but currently, *i.e.* spring 2012, telephone units are also introduced.

When the first mobile phones were introduced there were no exposure SAR limits. EU released a Council recommendation (1999/519/EC) of 12 July 1999 on the limitation of the exposure of the general public to electromagnetic fields (0 Hz- 300 GHz). This limited the local SAR value to 2 W/kg for the general public. Measurements on GSM and UMTS phones, at full output power, show that the local SAR value can be typically from a few tenth of a W/kg up to close to the 2 W/kg limit. The *actual* exposure from putting the mobile phone to the ear varies however considerably, between the different mobile phone generations, due to output power regulation.

The first generation did not use power regulation and the average output power was 1 W, so the actual exposure was highest for this system. As most of the early telephones were introduced before the SAR limits existed, it is not unlikely that the exposure could exceed the basic restriction of 2 W/kg.

The GSM system uses power regulation, which means that output power of the phone is regulated to maintain a connection with the base station. When the user is close to a base station the output power of the phone is down-regulated. Measurements have shown that the median pulse output power from GSM 900 unit is 0.1-0.2 W in cities, but in rural areas the median output is 2 W (which is the maximum output power), due to longer distance between the base stations (Lonn et al., 2004).

In the Interphone study more than 500 volunteers in 12 countries used GSM software modified phones for approximately 1 month each. These modified phones allowed the output power to be registered. Measurements of over 60 000 phone calls showed that the average output power was approximately 50% of the maximum, and that the output power varied by a factor of up to 2 to 3 between study centres and network operators (Vrijheid et al., 2009b).

The maximum average output power from UMTS phones is the same as for GSM 900 phones. However, the actual output power, in real use, is much lower for UMTS phones. Measurements in the Swedish UMTS network show a

median output power of 0.02 mW in cities and 0.04 mW in rural areas, (Persson et al., 2011).

Also the exposures from other sources have changed during the last 10 years. Analogue television has been replaced by digital television broadcasting, which usually have resulted in decreased total output power. On the other hand the use of WLAN has increased during the period. When measurements of exposure were repeatedly done in random locations in the Gothenburg area (26 locations in 1999, 48 in 2004, and 48 in 2011) there was no substantial difference in the average power density between the years, see Figure 1, (Hamnerius, 2011). The exposure level was highest in 2011, lowest in 2004 with 1999 in between. However, not all measurement points were identical in the different years. Most of these measurement sites were outdoor locations. The subset of indoor measurements did indicate an increase in exposure over the years. The majority of the measured exposure (78%), in the Gothenburg study, came from mobile phone systems, GSM 900, GSM 1800, UMTS and LTE, see Figure 2

This is in contrast to the results from the German study on exposure in bedrooms, where DECT and WLAN were the dominating sources (Breckenkamp et al., 2012). The explanation is probably that DECT and WLAN transmitters are usually located inside the residences and therefore dominates the exposure in bedrooms. Mobile phone base stations, on the other hand, are mostly located outdoors, and were therefore the dominating sources in the Gothenburg study, where most measured locations were outdoor.

Outdoor urban mean values 209-569 $\mu\text{W}/\text{m}^2$ were measured when exposimeters were used in studies performed in 5 different European countries (Joseph et al., 2010), these exposure levels are similar to the levels measured in the Gothenburg study. Frei and colleagues used exposimeters to assess the radio frequency exposure of 166 volunteers in Basel, Switzerland (Frei et al., 2009). The mean personal exposure was 130 $\mu\text{W}/\text{m}^2$. Exposure was mainly due to mobile phone base stations (32.0%), mobile phone handsets (29.1%) and wireless phones (DECT) (22.7%). Persons owning a DECT phone or mobile phone were more exposed. Mean values were highest in trains (1160 $\mu\text{W}/\text{m}^2$), airports (740 $\mu\text{W}/\text{m}^2$) and tramways or buses (360 $\mu\text{W}/\text{m}^2$) where exposures from other persons' mobile phones are common.

Although a substantial change in the dominating sources of RF exposure has occurred during the last decade, the total background exposure is still more than 1000 times lower than the ICNIRP reference values. GSM phone users can be locally exposed to values close to ICNIRP guidelines, when using the phone, while UMTS phone users are exposed to levels that are typically more than

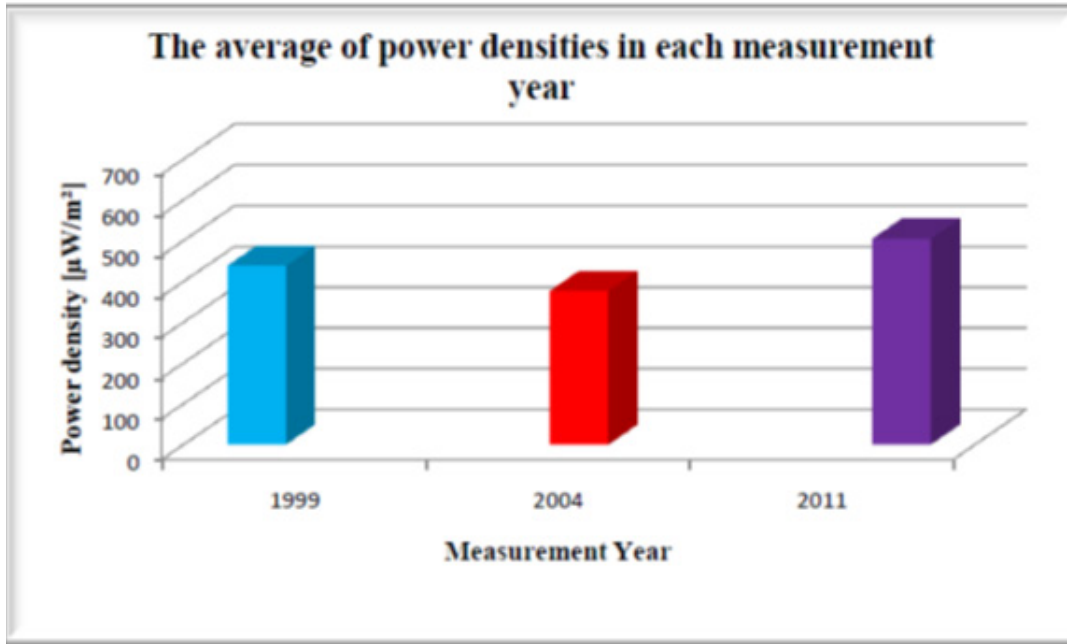


Figure 1. Average power density, 80 MHz – 2600 MHz, in mostly outdoor locations of the Gothenburg area, measured three different years.

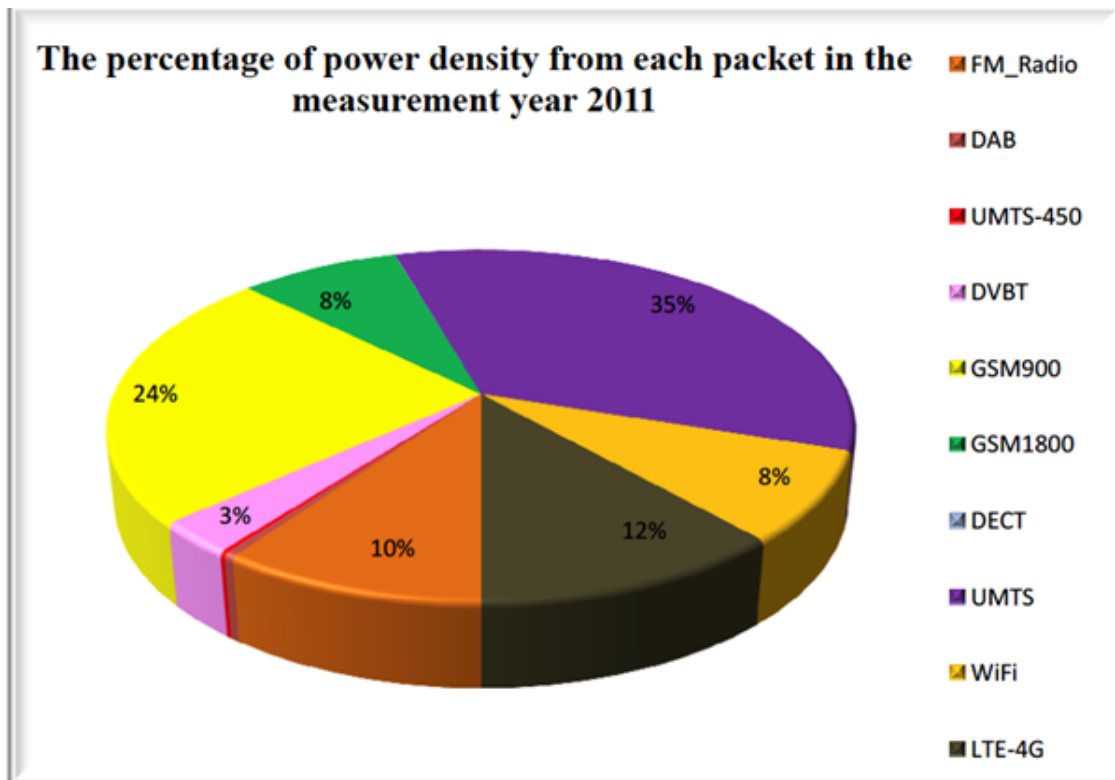


Figure 2. The distribution of measured exposure from different sources measured at 48, mostly outdoor, locations in the Gothenburg area.

1000 times lower. Thus the local exposure to the head from mobile phone use has been substantially reduced going from the NMT to the GSM and to the UMTS system. During the last decade there has also been a substantial change in mobile phone usage patterns. In 2003, the total number of outgoing calls with a mobile phone in Sweden was almost the same as the total number of calling time minutes (PTS, 2010). In 2009, the number of outgoing calls had not quite doubled compared to 2003, while there had been more than a fourfold increase in the total number of calling time minutes. The greatest change has, however, been for the number of text messages sent; from being about half as many as the number of outgoing calls in 2003, the number of SMS sent in 2009 by far outnumber both the total number of calls and total number of calling time minutes.

WHAT DO WE KNOW TODAY?

Thanks to developments in computational dosimetry it is now possible to determine the distribution of the absorbed RF power in different parts in the body.

The development of new body-worn measurement instruments, which can log the RF exposure, makes it possible to assess the individual exposure. This is a very valuable tool in epidemiological studies.

Measurements of RF exposure from distant sources show that the levels are more than 1000 times below the ICNIRP guideline.

The dominating exposure for most persons is from using his/her own mobile phone. For NMT and GSM phones this exposure can be in the same range as the ICNIRP guidelines basic restrictions for the general public. For UMTS this exposure is typically a factor 1000 lower. A UMTS phone does not, however, always secure a low exposure, as UMTS phones usually also has a GSM receiver built in. Which system is used depends on several factors, e.g. if UMTS coverage is missing, the GSM receiver is automatically used.

Apart from the exposure from the person's own phone the dominating exposure sources at outdoor locations are other persons' mobile phones and mobile phone base stations. For indoor locations WLAN and DECT systems often dominates.

Because historical data on exposure to the population are scarce it is not possible to assess any trends in exposure, or lack thereof, with certainty.

Symptoms attributed to radio-frequency field exposure

A small proportion of the population attributes a variety of acute, non-specific symptoms, such as headache, nausea, concentration difficulties, sleep disturbance, and fatigue, to electromagnetic field exposure. The types of symptoms vary between individuals and scientific studies have not been able to identify any specific symptom profile for persons who perceive themselves as hypersensitive to electromagnetic fields (Eltiti et al., 2007; Hillert et al., 2002; Osterberg et al., 2007). Reported symptoms can sometimes be very debilitating and have implications for the persons' quality of life, and a considerable amount of research has been performed to find out if electromagnetic field exposures are related to these conditions. The lack of objective signs of the condition has made it difficult to characterize these patients, and the condition has been described only on the basis of "self-diagnosis", i.e. "those who claim to have symptoms from EMF are EMF sensitive". Reported triggering factors (e.g. computer screens, fluorescent lights, electrical appliances in general, mobile phones and base stations) vary from individual to individual. Different operational definitions are used in studies trying to learn more about this condition. WHO states that it is not a medical diagnosis, nor that it is clear that it represents a single medical problem (WHO, 2005).

Although the challenge to find the underlying cause for perceived electromagnetic hypersensitivity has remained much the same the last 25 years, the focus for research on triggering factors has changed from extremely low frequency fields in the 1980s and 1990s to radiofrequency fields in the last decade.

Studies in experimental settings where the participants are tested under different conditions are well suited to investigate acute effects such as symptoms attributed to EMF exposure. These studies are often called provocation studies since the aim is to investigate whether a certain exposure or situation provokes a reaction. Ideally, provocation studies are performed double-blindly, i.e.

neither the participant nor the researcher is aware of actual exposure conditions during the tests. This will minimize the risk that expectations will influence the degree of symptoms or interpretation of results. Some studies have a single-blind design where only the participants are unaware of the exposure conditions.

WHAT DID WE KNOW 10 YEARS AGO?

At the time of the first report to FAS in 2003 (FAS, 2004) there were very few studies on symptoms attributed to radiofrequency fields. Research on perceived sensitivities to EMF fields had been initiated after reports of skin symptoms in relation to work with computer screens in the early 1980s (Knave et al., 1985; Linden and Rolfsen, 1981; Nilsen, 1982). Electromagnetic fields emitted by the screens were suggested to be the causal factor. In the late 1980s focus was turned to exposure from electric equipment in general and symptoms such as headache, difficulties concentrating and fatigue (Knave et al., 1989).

Early research on perceived electromagnetic hypersensitivity

Up to 2002, health problems attributed to computer screens or perceived general hypersensitivity to EMF were tested in more than 20 blind or double-blind scientific studies (Rubin et al., 2005). The exposure was mainly fields relevant to computer screens or electrical appliances.. The number of participants per study varied between one and 100. In theory, it would be enough to identify one person who reproducibly reacts to lower levels of EMF exposure than is today known to be perceived or cause health effects, in order to falsify the assumption that electromagnetic hypersensitivity does not exist. However, such a person has not yet been identified. Most studies have included groups of subjects who perceive themselves as hypersensitive to electromagnetic fields and have compared e.g. number or degree of symptoms occurring during exposure to EMF with those occurring when there is no exposure (so called sham exposure). While there was some variation

across tests and subjects, there was overall no support for a relationship between EMF exposure and symptoms in these studies (Rubin et al., 2005). There were also a few studies (Ofstedal et al., 1999; Ofstedal et al., 1995; Skulberg et al., 2001) that evaluated effects of reduction of EMF exposure in the workplace (e.g. by filters on computer screens), but there were no support for a beneficial effect on wellbeing from such interventions.

The Swedish Council for Work Life Research was commissioned by the Swedish government in 1997 to present a research review and evaluation of the results of Swedish and international research on “electromagnetic hypersensitivity” and health risks posed by electric and magnetic fields (1 Hz to 300 GHz). The report concluded that results of scientific studies suggest that electric or magnetic fields are neither sufficient nor necessary factors for triggering symptoms among individuals who perceive themselves as hypersensitive to electromagnetic fields and that research had not been able to identify any single factor of importance for the appearance of adverse health in these individuals (Bergqvist et al., 2000).

Early research on symptoms attributed to radiofrequency fields

Parallel to the introduction and spread of mobile telephony, discussions were initiated about possible health effects of radiofrequency fields other than those initiated by heating. In 2000, an independent expert group chaired by Sir William Stewart published the report *Mobile Phones and Health in the UK* (IEGMP, 2000a), usually referred to as the *Stewart report*. The expert group had heard several reports of mobile phone users who claimed that they had symptoms related to mobile phone use, but no systematic scientific studies were available at the time. For future research the Stewart report proposed double-blind studies to assess the relation of mobile phone use to symptoms, and that “highly sensitive” individuals in particular should be tested under double-blind conditions. Also the Swedish review noted that knowledge was limited regarding RF fields relevant to mobile telephony (Bergqvist et al., 2000).

By 2002 there was one scientific publication on RF exposures and symptoms (and detection of fields) that included subjects reporting to be sensitive to this exposure (Hietanen et al., 2002). No effect of RF exposure on symptom formation or any better ability than expected by chance to detect exposure to RF was found.

Thus, ten years ago a considerable number of provocation studies and other studies had found no evidence that exposure to ELF and intermediate frequency fields have the ability to trigger acute symptoms or ill health, but there were still very little data regarding RF exposure, and mobile phone use in particular.

WHAT DID WE LEARN DURING THE LAST 10 YEARS?

Several studies have tried to estimate the prevalence of perceived electromagnetic hypersensitivity. Considering the lack of objective measures of the condition and consensus on an operational definition, prevalence measures are difficult to interpret and compare. Levallois and coauthors reported a prevalence of “electromagnetic hypersensitivity” in California of 3% (Levallois et al., 2002), while Hillert and coworkers found that 1.5% of respondents in a cross-sectional survey in Stockholm county perceived themselves as electromagnetic hypersensitive (Hillert et al., 2002). The corresponding proportion in Switzerland was 5% (Schreier et al., 2006), in England 4 % (Eltiti et al., 2007) and Germany 10% (Blettner et al., 2009).

Different approaches have been used to assess whether RF exposure can cause the symptoms described by individuals who perceive themselves as hypersensitive to electromagnetic fields. A large number of experimental studies (single- or double-blind provocation studies) are now available. They have investigated whether RF exposure causes acute effects and whether individuals who perceive themselves as electromagnetically hypersensitive can detect the presence of RF exposure better than others. This study design is ideal when individuals report that they experience symptoms soon after having been exposed. To address potential delayed effects, observational studies have been performed.

Experimental studies of perceived hypersensitivity, symptoms and detection

During the last decade more than 15 single- or double-blind provocation studies have been published that have investigated potential effects of exposure to radiofrequency fields relevant to mobile phone use or exposure from base stations, that included participants who perceived themselves to be hypersensitive to electromagnetic fields or reported symptoms in relation to mobile phone use (Roosli et al., 2010a; Rubin et al., 2010). Apart from symptoms and detection of exposure, several studies also included cognitive and physiological effects that might be related to reported symptoms.

The studies generally included analyses of a large number of outcomes and exposure circumstances. Typically, participants did experience symptoms during the tests, especially those who reported being hypersensitive to RF fields, but in general independently of whether the fields were turned on or off (Roosli et al., 2010a; Roosli and Hug, 2011; Rubin et al., 2005; Rubin et al., 2010). A few of the studies reported a change in one out of many (up to 50) studied outcomes during exposure, but there is a lack of consistency between studies regarding which specific outcome was affected. In addition, the observed effect was as often beneficial (e.g. reduced symptoms) as adverse (e.g.

increase in symptoms). Similarly, a few effects were seen in the groups of healthy volunteers, which speak in favor of alternative explanations for these findings, such as the order of exposure or chance findings. When previously reported effects of RF exposure on symptoms or wellbeing were tested in new studies the initial observations were not confirmed (Eltiti et al., 2007; Regel et al., 2006; Zwamborn et al., 2003).

To address the concern that the artificial situation of being exposed in a laboratory might hamper the ability to detect an effect of the exposure, a German double-blind provocation study was performed as a field study. An experimental mobile phone base station (GSM 900 and 1800 MHz signals) was brought into 10 villages where no mobile phone service was available. The base-station transmitted in test mode without service, and therefore the signal could not be detected by ordinary mobile phones. Participants were either exposed or sham exposed for five consecutive nights each in a random order (Danker-Hopfe et al., 2010). There were no associations between nights with RF exposures from the experimental base station and sleep quality (sleep latency, total sleep time, wake after sleep onset and sleep efficiency index), neither in analyses of self-reported, nor of objective sleep data (electroencephalography, EEG, recording of electrical brain activity). Rated restfulness in the morning did not differ between the exposure conditions. In analyses restricted to nights with sham exposure (i.e. when the base station was inactive) participants who were concerned about possible health effects from base stations displayed worse sleep quality, not only in self-reported sleep data but also physiologically measurable by EEG, compared to participants who were not concerned.

One study investigated the effect of reduced exposure to RF fields. In a double blind study Leitgeb and coworkers (2008) used shielding material to reduce exposure to radiofrequency fields from base stations during the night (Leitgeb et al., 2008). No effect on sleep physiology or self-rated sleep was identified.

Several studies investigated whether persons who perceive themselves to be hypersensitive have a better ability than a control group to detect exposure to RF fields based on any perception of the fields (Rubin et al., 2010). No such difference was identified. In one study with young healthy adults, (some of whom reported being sensitive to RF fields) two participants had a very high proportion of correct responses (94% and 97%), but when they were retested, these results could not be replicated (Kwon et al., 2008).

Taken together, scientific studies have failed to provide support for a causal link between exposure to RF fields and wellbeing. Rubin and co-workers have published two

reviews on provocations studies (Rubin et al., 2005; Rubin et al., 2010). Of the 46 studies included in these reviews thirteen used RF exposure relevant to mobile phone handset exposure and six a base station like RF exposure). Altogether 1175 subjects who perceived themselves to be hypersensitive were tested. The conclusion in both reviews is that there is no scientific support for the theory that RF fields trigger symptoms. Other reviews have come to the same conclusion (Roosli et al., 2010a; Roosli and Hug, 2011). Augner and coworkers performed a meta-analysis on different outcomes, e.g. symptoms, cardiovascular effects, respiration and detection (Augner et al., 2012). Results from 17 studies (1174 participants) published between 2001 and 2010 were included in the analysis. No effects of RF fields were found.

Experimental studies on physiological effects

It is of interest to study physiological reactions in persons who perceive themselves as hypersensitive to RF or other electromagnetic fields, as possible mediators of reported symptoms. A recent systematic review of EMF exposure and physiological or cognitive effects in people who report electromagnetic hypersensitivity identified 13 studies of RF exposure relevant to mobile telephony (Rubin et al., 2011). The authors of the review concluded that there was no reliable evidence of any physiological effect of RF exposure specific to subjects who report being sensitive to electromagnetic fields.

The studies generally included a large number of analyses of possible effects, and a few associations were reported. One study reported a reduced heart rate and lower blood pressure associated with exposure (Hietanen et al., 2002). This might, however, have been caused by an unbalanced order of exposure, as sham exposure was always first or second of three or four consecutive exposure sessions. A Swedish study observed an effect on sleep EEG both in persons who perceived themselves as hypersensitive to electromagnetic fields and in healthy volunteers (Lowden et al., 2011). These results are in agreement with some results on sleep EEG in studies on healthy volunteers and provide no support for unique reactions in subjects who regard themselves as hypersensitive to RF fields. The same research group also reported that spatial memory was improved during exposure to RF fields in the group who reported symptoms in relation to mobile phone use, but only to a level comparable to that of the control group (Wiholm et al., 2009). Another study found improvement on a memory test during RF exposure only in the control group (Zwamborn et al., 2003). The same or similar outcomes were assessed also in other studies without any effects being observed.

A meta-analysis of the impact of RF exposure from mobile phones on cognitive function included 16 studies on GSM exposure and 1 study on UMTS (Barth et al., 2012).

Only cognitive outcomes analyzed in at least two studies were considered. No effect of RF exposure on cognitive performance was identified.

In conclusion, there is no reliable evidence of any physiological or cognitive effects of RF exposure specific to subjects who report being sensitive to electromagnetic fields.

Physiological characteristics of individuals who perceive themselves to be hypersensitive to electromagnetic fields

While there is no consistent evidence that low-level EMF exposure influence physiological outcomes, it has been observed that there are EMF unrelated differences between subjects who perceive themselves to be hypersensitive to EMF and healthy controls. Differences in the autonomic nervous system were reported in several studies, e.g. regarding heart rate and blood pressure, indicating a shift towards sympathetic predominance in subjects reporting such hypersensitivity, see e.g. (Lyskov et al., 2001; Sandstrom et al., 2003; Wilen et al., 2006). A German fMRI (functional Magnetic Resonance Imaging) study analyzed brain activation during two conditions; heat and sham RF exposure (i.e. believed but no real RF exposure) (Landgrebe et al., 2008). The study included 15 subjects who perceived themselves to be hypersensitive to EMF (including RF fields) and 15 healthy controls. When participants were told that they would be exposed to RF fields (but with no actual exposure) the group with perceived hypersensitivity displayed an increased activation in certain parts of the brain (the anterior cingulate and insular cortex) compared to baseline as well as compared to the control group. In addition, reporting symptoms during sham exposure were associated with alterations in cortical activity in the same brain areas. The heat exposure, which was used as a positive control, led to similar brain activations in both groups as was expected.

Nocebo effects

A nocebo effect is an unwanted or unpleasant effect that is triggered by expectations that such an effect may occur, e.g. due to concern or earlier experiences (Latin Nocebo= I will harm). Several studies have shown that symptoms in individuals who perceive themselves as hypersensitive to EMF may be provoked by expectations. Participants reported reactions when there was no exposure, see e.g. (Rubin et al., 2005; Rubin et al., 2006) or when the participants were falsely told that they were being exposed (Landgrebe et al., 2008; Szemerszky et al., 2010). Sham exposure has triggered symptoms as often and to the same degree as exposure to RF fields in provocation studies. Szemerszky and coauthors showed that the degree of self-reported hypersensitivity to electromagnetic fields was associated both with expectations prior to the tests that more symptoms would occur and with more experienced

symptoms during the tests in a provocation study where the participants were falsely told they would be exposed to EMF (Szemerszky et al., 2010). More symptoms were reported during the tests when the participants were told that the EMF exposure would be strong as compared to when they were told the exposure would be weak. The fMRI study by Landgrebe and coworkers (2008) described above, provides further support for a nocebo effect by demonstrating changes in cortical activity when participants who perceived themselves to be hypersensitive to RF fields were falsely told they would be exposed. Some studies included open provocations prior to the blinded tests. The potential participants were thus given the opportunity to test, knowing they would be exposed, if they reacted to the exposure to be included in the double-blind tests, e.g. (Oftedal et al., 2007). Even though a relationship between exposure and self-reported reactions were reported in the open tests, no such relationship was found in the double-blind tests. These results indicate that expectations alone are sufficient to trigger symptom formation.

Observational studies of perceived hypersensitivity and symptoms

Cross sectional studies

Most observational studies within this area of research have used a cross sectional design. Cross-sectional studies are of limited value when investigating causal relationships. Exposure is assessed at the same time as the outcome of interest without taking the temporal relation into consideration. In addition, exposure estimates have often been based on self-reported information. Thus, the cross-sectional studies may be affected both by reversed causality, i.e. that the outcome affects the exposure rather than the opposite, and by recall bias. Furthermore, low response rates may lead to substantial selection bias which may distort results. There is evidence that persons who are concerned about mobile phone exposure are more likely to participate in a study, and also more likely to have identified potential exposure sources, such as mobile phone base stations (Thomas et al., 2008b).

Environmental RF exposure

Until 2010, all epidemiological studies on symptoms and environmental RF exposure, e.g. from base stations, were cross-sectional. While self-reported exposure to RF fields, e.g. estimated distance to nearest base station, was often associated with more symptoms, sleep problems or reduced wellbeing, see e.g. (Baliatsas et al., 2011; Blettner et al., 2009; Navarro et al., 2003; Santini et al., 2003), no consistent effect on symptoms or wellbeing has been observed when RF exposure or distance to base station was measured objectively, see e.g. (Baliatsas et al., 2011; Berg-Beckhoff et al., 2009; Heinrich et al., 2010, 2011; Thomas et al., 2008a), or estimated based on e.g. geographical information and considering factors that were shown to

have a significant influence on the exposure to RF fields, e.g. TV- and radio transmitters, building characteristics (Mohler et al., 2010). In the study by Mohler et al. 18% attributed their own adverse health effects to RF exposure, while 8% perceived themselves as being hypersensitive to electromagnetic fields. The authors found no indication that RF exposure affected individuals with perceived hypersensitivity differently than others.

A study on children and adolescents, where personal exposure was assessed by exposimeters during 24 hours, found no convincing support for an RF effect on acute symptoms or chronic well-being (Heinrich et al., 2010, 2011). Berg-Beckhoff and coworkers (2009) measured exposure to RF fields in the homes of the participants. By analyzing different frequencies it was possible to differentiate between different sources of the fields, e.g. mobile phone handsets, base stations and TV-antennas. Fields from mobile phones were excluded in order to investigate possible health effects from other environmental RF sources. No effects of exposure to RF fields from mobile phone base stations or other environmental sources were observed with regard to health complaints and sleep. Self-reported sleep problems and health complaints were on the other hand related to the attribution of health disturbances to base stations. About 9% of participants attributed health and sleep problems to RF exposure.

RF exposure from mobile phone use

During the last 10 years a number of cross-sectional studies of mobile phone use and symptoms have been published, and many of them report an association between self-reported mobile phone use and various symptoms, see e.g. (Balik et al., 2005; Balikci et al., 2005; Khan, 2008; Soderqvist et al., 2008), although not all (Mohler et al., 2010; Mortazavi et al., 2007).

These cross-sectional studies have, however, major limitations, as discussed above. Recall bias is a severe problem, and non-participation might have caused selection bias, especially if the purpose of the study was revealed to participants. Reversed causality is a greater problem in studies where exposure is controlled by the individuals themselves (i.e. mobile phone use). Apart from these methodological limitations with the cross-sectional design, potential confounding factors that might affect the results were not controlled in the analyses, such as socioeconomic status, level of stress, working hours, life-style etc., i.e. factors that are likely to affect both the amount of mobile phone use and health outcomes such as sleeping problems, concentrations difficulties etc. Studies have shown that other aspects of mobile phone use may give rise to similar health complaints as those reported by individuals who perceive themselves as electrically hypersensitive, and may thus be confounding factors in studies of effects of RF exposure. These are for example

being awakened at night by calls or text messages, stress associated with demands of constant availability, unhealthy sleeping habits (Punamaki et al., 2007; Thomee et al., 2011; Van den Bulck, 2007).

Prospective study

Only one prospective cohort study of RF exposure and symptoms has been performed. Rösli and coworkers followed 1122 participants from 2008 to 2009 (Frei et al., 2012; Roosli et al., 2010b) with regard to changes in perceived health, measured through questionnaire based scales capturing e.g. fatigue, loss of appetite, lack of energy or concentration, headache. Among participants, 130 persons perceived themselves as hypersensitive to electromagnetic fields either at baseline or follow-up, and in addition 219 attributed their symptoms to “electromagnetic pollution”, but did not define themselves as “electrohypersensitive”. Exposure to RF fields was calculated based on a validated method including information on radiofrequency transmitters and base stations, building characteristics of homes and amount of time the subject spent indoors, as well as use of mobile and cordless phones. Exposure to RF fields was also estimated as self-reported mobile and cordless phone use and operator recorded mobile phone use. In addition, participants were asked to rate if their personal exposure situation was lower, the same, or higher than the average Swiss population. The study found no association between calculated total RF exposure at baseline and change in reported symptoms during the study period. This was true for the whole study group as well as the group who perceived themselves to be hypersensitive to RF fields, or attributed symptoms to EMF. Individuals who were in the highest exposure category of self-reported mobile phone use at base-line reported improvement in health at follow-up. Those who self-rated their personal exposure as higher than the average Swiss population as baseline reported an increase of symptoms at follow-up. This analysis was made as an assessment of a possible placebo effect or recall bias. Overall, the results do not support the hypothesis that RF exposure causes non-specific symptoms.

WHAT DO WE KNOW TODAY?

During the last 10 years the knowledge base concerning self-reported “electromagnetic hypersensitivity” has grown to include a large number studies on radiofrequency fields and symptoms as well as new knowledge on possible physiological reactions. Despite considerable research efforts during the last 10 years, no association between radiofrequency fields and wellbeing has been established. Radiofrequency fields have not been shown to trigger symptoms in subjects who perceive themselves as hypersensitive to RF fields and this group has not displayed any better ability to detect exposure to electromagnetic fields than reference groups that do not report this type of sensitivity. Sporadic reported effects of RF fields on single

outcomes have been inconsistent and not confirmed in new studies or retests of possibly sensitive subjects.

No biological marker of perceived hypersensitivity to EMF or physiological reaction specific to the group who reports electromagnetic hypersensitivity has been identified.

The fact that scientific studies have failed to confirm the proposed relationship between RF fields and symptoms, in combination with results showing that effects are triggered when subjects believe or know that they are being exposed, has led to the proposal that a nocebo effect may be at work (WHO, 2005, Oftedal et al., 2007, Rubin et al., 2006, Rubin et al., 2010). It should be stressed that the support for a nocebo effect is based not only on the lack of support for a direct causal effect of RF fields but also on several studies that displayed effects of anticipation and expectation of being exposed while no active exposure was present.

RF exposure and cancer risk – evidence from epidemiological studies

WHAT DID WE KNOW 10 YEARS AGO?

In the beginning of the 2000s only a few epidemiological studies on mobile phone use and cancer risk were available, and the evidence from investigations of exposures in occupations and from transmitters was very limited (Ahlbom et al., 2004). In general, the epidemiological studies of RF exposure in occupations and from transmitters suffered from poor and imprecise exposure assessment, and mobile phone use had only recently become prevalent in the general population. The research was performed as the result of public concern; no mechanism for a carcinogenic effect had been identified and there was no suggestive evidence from experimental studies. It was nevertheless judged important to carry out research on possible health effects of RF exposure, considering the rapid increase in the prevalence of mobile phone use worldwide.

The first studies of mobile phone use and brain tumor risk was published in the late 1990s and early 2000s. Considering the short time period during which mobile phones had been available, the studies at the time could only provide evidence of relevance for short latency periods. They generally reported no overall risk increase for brain tumors, although subgroup analyses in one study found an increased risk for brain tumors in the temporal or occipital lobe, including in this subgroup also temporoparietal locations, as well as related to which side of the head the phone had been used (Hardell et al., 1999). With no overall risk increase these results appeared less convincing, and the methods and presentation of the study were criticized (see e.g. (AGNIR, 2003)).

Most occupational studies focused on the risk of cancer overall, and leukemia and brain tumors (Ahlbom et al., 2004). No consistently increased risks were reported, but findings were often based on small numbers, and

exposure assessment was crude. A few risk increases were observed, generally in studies with severe methodological shortcomings. These studies are described in detail for example in Ahlbom et al., 2004 and AGNIR, 2003. Overall, the data did not suggest an increased cancer risk associated with occupational RF exposure, but the evidence was not sufficient to exclude the possibility of a risk increase. Since then, only few occupational studies have been published, and they do not change the overall assessment. Therefore, occupational exposures will not be further discussed in this report.

Studies of environmental RF exposure from transmitters, i.e. radio- and television transmitters, were even fewer and also based on small numbers of exposed cases (Ahlbom et al., 2004). They were generally of ecologic design, preventing any conclusions on cause and effect. In the early 2000s there were no studies available on cancer risk related to exposure from mobile phone base stations.

Independent expert groups concluded that the balance of the evidence suggested that RF exposure below guideline levels do not cause adverse health effects, but identified gaps in the knowledge and recommended further research (AGNIR, 2003; Health Council of the Netherlands, 2002; IEGMP, 2000b). National research programs were established in several countries, e.g. Denmark, Finland, Great Britain, France, the Netherlands, and Switzerland. In addition, the European Union funded both epidemiological and experimental studies focused on possible effects of RF exposure on cancer related outcomes. This increased the total amount of funding available for scientific research within the area, and as a result, the pool of data has increased substantially, both in terms of amount and generally also in quality.

WHAT HAVE WE LEARNED DURING THE LAST 10 YEARS?

Methodological issues

Most of the studies on mobile phone use and brain tumor risk have been case-control studies with retrospectively collected self-reported information on past mobile phone use, an exception being the Danish cohort study of mobile phone subscribers. A major problem with the case-control design in this context is exposure misclassification, both non-differential and differential, where the former could lead to a dilution of an effect should there be a true association, and the latter could lead to reports of overestimated or even spurious effects. An additional problem is selection bias caused by non-participation.

The Interphone study is a large multinational collaborative study of mobile phone use and risk of tumors in the brain and salivary glands (Cardis et al., 2007). Within Interphone several validation studies were performed to assess the presence and magnitude of the influence of various types of biases in case-control studies. The results show that exposure misclassification is substantial even for recall as short as 6 months when comparing self-reported to independently recorded phone use (Vrijheid et al., 2006), and it seems to be more difficult to remember amount of time spent on the mobile phone than number of calls. Other studies have made the same observations, e.g. (Inyang et al., 2009). There is also evidence of recall bias; cases tended to overestimate their mobile phone use more the further back in time they were reporting about, a tendency that was not observed among controls (Vrijheid et al., 2009a). Of note is that the time period for which operator data were available was no more than around 4 years, while case-control studies try to estimate mobile phone use more than 10 years prior to diagnosis. Also, reports of implausible amounts of use were more common among cases than among controls (The Interphone study group, 2010).

An additional challenge in studies of brain tumor risk is the need for rapid ascertainment of the patients because of the poor prognosis associated especially with malignant brain tumors. It is very difficult for close relatives to know and report retrospectively about the amount of time their deceased relative had used a mobile phone many years before he/she was diagnosed with a brain tumor. This is illustrated in a study of deceased cases, originally diagnosed with a brain tumor between 1997 – 2003, and deceased controls (Hardell et al., 2010), where close relatives were contacted late 2006 – 2008 and asked to report about mobile phone habits of their deceased relative. Controls were persons who had died from other causes during the same time period as the brain tumor patients. The amount of mobile phone use reported by relatives to controls were about three times higher than the amount reported by the

controls included in the original studies (Hardell et al., 2006; Hardell et al., 2002), even though the reports were supposed to cover the same time period.

Another validation study within the Interphone study assessed potential selection bias caused by non-participation (Vrijheid et al., 2009c). It was found that among both cases and controls, mobile phone users were more likely to agree to participate, while non-users more often declined participation. As participation proportions were higher among cases than controls, it was estimated that this would lead to a downward bias of risk estimates by approximately 10%. Results of the Interphone risk analyses showed that the majority of risk estimates were slightly below one. Interestingly, this was true also in centers that did not mention in the introductory letter that mobile phone use was one of the risk factors of interest for the study.

The cohort study of mobile phone subscribers (Frei et al., 2011; Johansen et al., 2001; Schuz et al., 2006b) is not subject to recall bias, as exposure information is collected independently of the disease. The exposure parameter studied is time since first mobile phone use; no attempt was made to study amount of use. Follow-up of the cohort in the cancer registry does not require participation of the subjects and with access to a population based cancer registry of high quality and a continuously updated registry of the total population, selection bias is not a problem. Here the main potential source of bias is non-differential exposure misclassification. Being a mobile phone subscriber does not necessarily mean that a person is also a mobile phone user, although it seems less likely that a person would have a mobile phone subscription for someone else without being a mobile phone user him/herself. A more serious problem is the inability to link all the 720 000 mobile phone subscriptions in the country to an individual. In total, 420 000 mobile phone subscribers were identified, leaving around 300 000 unidentified subscriptions. Approximately 200 000 of these were corporate subscriptions. The total size of the Danish adult population without a known mobile phone subscription at the time was around 4 130 000 persons, which means that the unidentified mobile phone subscribers constitutes a maximum of 7% of the unexposed. Based on this information, one can easily estimate the magnitude of the effect of the non-differential exposure misclassification on the observed risk estimates. If one assumes that the true relative risk is 2.5, the misclassification would lead to an observed risk estimate of approximately 2.2. Because of the small proportion of mobile phone users in the population when the Danish subscriber cohort was established, the non-differential exposure misclassification will only have a marginal effect on the observed risk estimates.

Mobile phone use and cancer

In total, around 15 studies of mobile phone use and brain tumors have been published (Ahlbom et al., 2009; Swerdlow et al., 2011; AGNIR 2012), most of them focusing on glioma and acoustic neuroma, somewhat fewer on meningioma. Two were US studies with short latency periods, two registry based (subscriber registers), three Swedish studies from the Hardell group, and the rest national or regional Interphone studies. The national Interphone studies often included a wider age-range than stipulated by the common core protocol, and therefore, national Interphone publications need also be taken into consideration to cover all available data. Pooled analyses of the combined data from the two latest Hardell studies have been published in several papers, but results from these two studies differ considerably, as described below, and no homogeneity tests were presented. For glioma it seems likely that results differ more than would be expected by chance alone, and therefore we discuss only the original publications here, as they cover all available data.

In most studies, the main analyses were of exposure defined as time since first mobile phone use. Amount of use in cumulative hours or cumulative number of calls has also been analyzed in several of the studies, but cutpoints differ considerably between studies and were most often defined based on the distribution among the controls.

Time since first use

For glioma, most of the epidemiological evidence speaks against an increased risk associated with time since first mobile phone use, regardless of whether short-, intermediate- or long-term use. The longest latency period studied so far is in the Danish cohort study, where it was as long as at least 13 years since first mobile phone subscription, and no indication of increased risk was found (Frei et al., 2011). One exception to this pattern is the third study performed by Hardell and co-workers, where a 60% risk increase for glioma was observed after less than five years since first use of a digital mobile phone, and more than threefold after 10 years of use of digital or analogue mobile phones (Hardell et al., 2006). The second exception is the Interphone web-annex (The Interphone study group, 2010), where a 70% risk increase for glioma after less than five years, and 100% increase after 10 years, were reported in post hoc analyses restricted to regular users only, in an attempt to try to take selection bias into consideration. This method to adjust for selection bias is based on the assumption that selection bias is the only reason for the reduced odds ratios. There are strong reasons to believe that this is not the case, thoroughly discussed in the web-annex of the Interphone publication, and the adjustment will then lead to an upward bias of the risk estimates (The Interphone study group, 2010). None of the other studies, including also the main Interphone paper, found any increased glioma risk related to time since first use.

For meningioma, all studies reported risk estimates close to unity regardless of time since first use, except the third study by Hardell and co-workers where a twofold risk increase was reported after 10 years since first use of an analogue phone (Hardell et al., 2005). For acoustic neuroma the pattern is virtually the same, except that both the second and third studies performed by Hardell and co-workers reported increased risks of considerable magnitude already after less than five years of mobile phone use (Hardell et al., 2005; Hardell et al., 2002), e.g. a three- to nine-fold risk increase.

One difference between the studies by Hardell and co-workers and other studies is that Hardell et al. takes cordless phone use into consideration in the analyses of mobile phone use, i.e. persons who do not use mobile phones but are cordless phone users are not included in the unexposed category as they are in other studies. Cordless phone use have been analyzed in two of the national Interphone studies (Lonn et al., 2005; Schuz et al., 2006a), and none of them found any association with brain tumor risk. The German study analyzed a combination of cordless and mobile phone use (Schuz et al., 2006a), similar to the analyses in the Hardell studies, but still found no associations. In addition, when Hardell and colleagues included cordless phone users into the unexposed category to mimic the analyses in the Interphone study, the results were virtually unchanged (Hardell et al., 2011b). Thus, cordless phone use does not explain the differences in results between the studies by Hardell and colleagues and other studies.

The few reported risk increases appear implausible for several reasons. If they were real, an increased incidence of glioma and acoustic neuroma would have been observed in cancer registry data. As discussed below, the glioma incidence has been stable since the introduction of mobile phones, and the acoustic neuroma incidence has increased far below what would have been expected based on the reported findings in the Hardell et al. studies. Second, as acoustic neuroma is a slow-growing tumor, one would not expect an effect on the tumor occurrence after such a short latency period. It is likely that most of the acoustic neuroma tumors occurring within five years since first mobile phone use were already present when the person started to use a mobile phone (Thomsen and Tos, 1990).

Amount of mobile phone use

In the Interphone study, amount of mobile phone use was analyzed in 10 exposure categories, corresponding approximately to the distribution in deciles among controls. No trends of increasing risk with increasing cumulative hours of use or number of calls were observed for any of the studied outcomes (Interphone study group, 2011; The Interphone study group, 2010). In the highest exposure category, ≥ 1640 hours of use, a slight risk increase

was observed for all three outcomes, 1.40 for glioma, 1.15 for meningioma, and 1.32 for acoustic neuroma. It is noteworthy that the risk estimates in the 9th decile (735–1639 h) were among the lowest observed, 0.71 for glioma, 0.76 for meningioma, and 0.48 for acoustic neuroma. For glioma and meningioma the highest risk increase associated with heavy mobile phone use was observed mainly among short-term users, for acoustic neuroma among long-term users. No associations were observed with cumulative number of calls.

The third study by Hardell and co-workers also reported increased risks associated with amount of use (Hardell et al., 2005; Hardell et al., 2006), but at much lower levels than in Interphone. A four-fold risk increase of malignant brain tumors was observed for >80 h of analogue phone use (cutpoint at the median of the distribution among controls), and 2.4 fold for >64 h of use of a digital phone. For meningioma the corresponding results were about two-fold for both types of phones, and for acoustic neuroma the risk increase was 6-fold for >80 h of use of an analogue phone and 2.5 fold for >64 h of use of a digital phone. Several other studies have analyzed higher amounts of use than those reported in the Hardell study, e.g. the two studies from the US (around 500 h as the highest cutpoint), and national Interphone studies (>500 h), but none of these studies found increased risks at these levels of use.

The very high risk increases at quite low amounts of mobile phone use reported in the study by Hardell et al. appear implausible in the light of the stable incidence trends, and deviates from findings in all other studies. Also, the reported increased risks in the highest decile in the Interphone study appear unlikely to be causal, considering the lack of dose-response and the very low risk estimates in the 9th percentile; for acoustic neuroma almost a downward trend until the 10th percentile. In addition, there were more frequent reports of implausibly high cumulative hours of use among cases than controls. The results from the validation study provide empirical evidence that recall bias is likely to have affected the findings (Vrijheid et al., 2009a), but the question is whether it can explain the small risk increase completely.

Laterality of phone use

Radiofrequency exposure to the head is highly localized during mobile phone use, and reaches only a few centimeters into the brain. Therefore, if the exposure is causally related to brain tumor risk, one would expect to find a risk increase on the same side of the head as the phone was usually held, and a risk close to unity on the opposite side. Information about laterality of phone use has so far only been collected retrospectively, and no validation study have been performed to assess cases' and controls' ability to correctly report on past side of

phone use. There is a possibility that cases' answers to the question on which side the phone was usually held prior to diagnosis are affected by their knowledge about the side of the tumor location, and they might tend to more often report ipsilateral use (Schuz, 2009). Controls have no corresponding knowledge, and will report independently of the assigned "tumor" side. Results in the case-control studies indicate that this might have happened. In the absence of an overall risk increase, findings of an increased risk for ipsilateral use must be accompanied by a reduced risk somewhere else. Indeed, several studies found an increased risk of brain tumors on the same side of the head as the phone was reported to be held, and at the same time a reduced risk on the opposite side and/or among subjects for whom laterality data were missing (Ahlbom et al., 2009; Schuz, 2009; Swerdlow et al., 2011). For example in the Interphone study, almost all risk estimates for ipsilateral phone use were higher than those for contralateral use, also in exposure categories with very short latency and very small amounts of use. For glioma, among the highest ratios of ipsi- to contralateral use were found for less than 2 years since first mobile phone use and less than 5 h of cumulative use. The rare exception to this pattern is the third study by Hardell and co-workers (Hardell et al., 2005; Hardell et al., 2006), where increased risks of the same magnitude were reported for both ipsi- and contralateral use. Overall, there are strong indications that recall bias may have affected results where laterality were taken into consideration.

Lobe specific results

Another attempt to take the localized exposure into consideration has been to perform lobe specific analyses. The lobes considered to be the most highly exposed have not, however, been consistent between studies, although all have included the temporal lobe, sometimes along with various other locations. For glioma, most studies have not found higher risk estimates for tumors in the temporal lobe than in other locations. The only exception is the Interphone combined analysis, where slightly higher risk estimates for tumors in the temporal lobe were found for long-term use and in the highest category of cumulative hours of use, but not overall (The Interphone study group, 2010). For meningioma, the same study found a much lower risk estimate overall for tumors in the temporal lobe than in other locations. The two latest studies by Hardell and co-workers did not find higher risk estimates for malignant tumors in the temporal lobe than in other locations (Hardell et al., 2011b; Hardell et al., 2006; Hardell et al., 2002). Taken together, the evidence does not suggest that mobile phone use is more strongly associated with tumors in the temporal lobe.

Tumor localization studies

Two studies have used information about the exact localization of the tumor based on radiological images (Cardis et al., 2011; Larjavaara et al., 2011b). One of the

studies used a case-case design to test the hypothesis that glioma in mobile phone users would on average be located closer to the exposure source, i.e. closer to where a phone is held, than tumors among cases who did not use a mobile phone regularly (Larjavaara et al., 2011b). This type of design eliminates potential selection bias caused by non-participation among controls, and reduces the effect of recall bias. Analyses were based on 873 glioma cases, and no major difference in distance between the tumor location and a hypothetical mobile phone was found between cases who were regular mobile phone users and those who were non-users; if anything the distance was somewhat shorter for non-users. The distance was longest among cases who had used a mobile phone longest and most intensive, although differences were small.

The other study estimated the total RF dose at the tumor location or a corresponding location for the controls (Cardis et al., 2011). The total RF dose was estimated based on self-reported information on cumulative hours of mobile phone use, frequency band, communication system, and network characteristics. Self-reported cumulative hours of use and tumor location were the only significant predictors of RF dose (43% and 13% of the variation, respectively). Complete data for estimation of RF dose were available for a subgroup of subjects, and results were almost identical when based simply on self-reported cumulative hours of use as when the more elaborated exposure measure was used, contrary to what would have been expected if there was a causal association between RF dose and brain tumor risk. The study design did not attempt to reduce recall bias, and the addition of more technical details about the mobile communication system did not seem to help advancing the knowledge of possible effects of RF exposure. The investigators also made a case-case analysis, similar to the analysis in the Larjavaara study, but based on somewhat fewer cases (556). They found that ≥ 10 years since first mobile phone use was associated with an increased risk of glioma in the brain region with the highest exposure, but also a decreased risk for those with 5 – 9 years since first use.

Children

There is currently only one study available on mobile phone use and risk of brain tumors in children and adolescents (Aydin et al., 2011). A risk estimate close to unity was observed, and risk did not increase with amount of use or by location of the tumor. In a subgroup analysis based on only about one third of the data, a duration of >2.8 years since first mobile phone subscription was associated with an increased brain tumor risk. This result was, however, not compatible with the stable incidence trends observed, as one would have expected an increase in childhood brain tumor incidence if this was a true finding. Thus, the study does not support the hypothesis of an increased risk of

brain tumors, but also does not provide strong evidence against a risk increase.

Other tumors

For other tumor types, e.g. parotid gland tumors, ocular melanoma, leukemia, lymphoma, and testicular cancer, the available data are considerably fewer than for brain tumors. Currently, no consistent evidence speaks in favor of the hypothesis that mobile phone use is associated with an increased risk of these tumors (Ahlbom et al., 2009; AGNIR 2012).

Transmitters and cancer

Currently, only a few studies are available where RF exposure from transmitters has been estimated on an individual level. Two studies have looked at RF fields from radio- and television towers in relation to childhood leukemia (Ha et al., 2008; Ha et al., 2007; Merzenich et al., 2008; Schuz et al., 2008), and one study on RF exposure from mobile phone base stations and childhood cancer risk (Elliott et al., 2010). None of the studies found any indications of increased risk for any types of tumors among children in relation to environmental RF exposure from transmitters.

Taken together, the evidence does not support the hypothesis that environmental RF exposure from transmitters affects cancer risk. The studies have, however, limited power to detect a small risk increase.

Incidence studies

During the last decades, there has been a rapid increase in the prevalence of mobile phone use in the general population in many countries, from a few percent at the end of the 1980s to near 100% in some age-groups by the first half of the 2000s. The Swedish Post and Telecom Agency (PTS) reported in 2003 that 90% of the Swedish population in the ages 16-79 years were mobile phone users (Post- och Telestyrelsen, 2003). If radiofrequency exposure from mobile phone use affects the risk of brain tumors, one would expect to see an increasing brain tumor incidence in many countries, unless the latency period is extremely long or the risk increase is restricted to a very small subgroup of the population. During the last few years, brain tumor incidence studies have been published from the Nordic countries, the UK, the US, and Australia (Ahlbom and Feychting, 2011; de Vocht et al., 2011; Deltour et al., 2011; Deltour et al., 2009; Dobes et al., 2011; Inskip et al., 2010; Kohler et al., 2011; Little et al., 2012). They have all reported on malignant brain tumors or glioma specifically, i.e. the tumor type for which increased risks have been reported in a few of the case-control studies. The time periods included differ between the incidence studies, but the majority covers the incidence until 2007 or 2008, one as long as 2009. All studies report stable incidence trends in

age-groups where mobile phone use has become prevalent, with no indications of increasing incidence after the introduction of mobile phones.

The Swedish Cancer registry has now updated information including 2010. There is still no upward trend in the glioma incidence rate in the age-groups where mobile phone use have been most prevalent, although a slight increase is seen between 2009 and 2010 in persons 60 years or older (Figure 3). The increased incidence in the oldest age-group could be real, but may also be the result of random variation or improved cancer registration. A validation study found that underreporting of nervous system tumors in the oldest age group was considerable (Barlow et al., 2009).

An increased risk in a very small subgroup of the population would not be detected in incidence trends, but so far, none of the epidemiological studies have reported an increased risk in such a small subgroup. Neither cohort, case-control or incidence studies performed to date would be able to detect a risk increase after an induction period exceeding 15-20 years. Experimental studies, including also animal studies with long-term exposure, have not found consistent evidence of a carcinogenic effect, and despite the large amount of research performed, a plausible biological mechanism has still not been suggested. Thus, the amounting evidence speaks increasingly against a carcinogenic effect of exposure to low-level radiofrequency electromagnetic fields.

A recent incidence study estimated the probability that the increased risks of glioma reported in a few case-control studies would have been detected as a significant increase in the glioma incidence rate in the Nordic countries, using data on prevalence of mobile phone use and incidence from cancer registers (Deltour et al., 2011). The results showed that a relative risk of 2.0 with an induction period of up to 15 years would have been detected with 100% probability, as well as a relative risk as low as 1.2 with up to 5 years induction period. For heavy mobile phone use, corresponding to the highest exposure category in the Interphone study (≥ 1640 cumulative hours), a relative risk of 2.0 with up to 5 years induction period would have been detected with 100% probability, and a relative risk of 1.5 with 98% probability. This means that the risk increases related to mobile phone use that have been reported in a few case-control studies would have resulted in a detectable increase in the glioma incidence in the Nordic countries, had they been real.

A study from the US used a similar approach, by calculating the predicted glioma incidence rates in the US based on the results from the pooled study of Hardell and co-workers and the Interphone study (Hardell et al., 2011a; Little et al., 2012; The Interphone study group, 2010). Results showed that the predicted glioma incidence rate using the results from the Swedish study (Hardell et al.,

2011a) would be at least 40% higher than was observed, while the modest risk increases in the Interphone study were compatible with observed incidence rates.

Several of the studies report also separately on brain tumor incidence trends for children and adolescents, 0-19 years (de Vocht et al., 2011; Dobes et al., 2011; Inskip et al., 2010). In addition, two studies have reported on incidence trends in the age group 5-19 years (Aydin et al., 2011; Boice and Tarone, 2011). None of these studies found increases in the brain tumor incidence after the introduction of mobile phones.

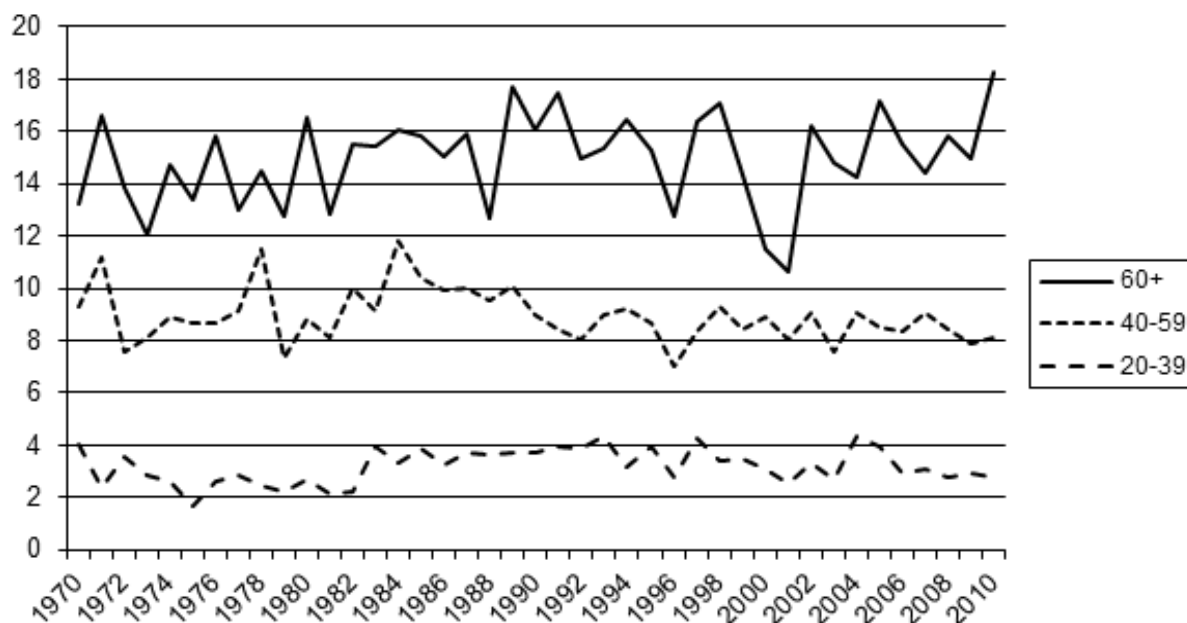
Larjavaara and co-workers found that the incidence of acoustic neuroma in the Nordic countries increased slightly between 1987 and the late 1990s, and stabilized or even decreased from the beginning of the 2000s (Larjavaara et al., 2011a). The total increase in the incidence over the period was 3%, which is not compatible with the high risk estimates associated with mobile phone use reported in a few case-control studies.

Some of the published analyses of incidence trends have severe methodological limitations. Lehrer and colleagues reported that the occurrence of brain tumors in the US increases with increasing numbers of mobile phone subscriptions (Lehrer et al., 2011). What they have shown, however, is essentially that both the number of mobile phone subscriptions and the number of brain tumor cases are correlated with population size (Boniol et al., 2011). Other reports, that are easily misinterpreted, analyze all central nervous system tumors combined, but refer to them as "brain tumors", e.g. based on data from NORDCAN (internet based data from the Nordic cancer registers). The NORDCAN data are of high quality, but include also benign tumors and nervous system tumors at other locations that are not particularly exposed during mobile phone use. Therefore, they provide limited information about trends in the glioma incidence rates. Other misleading statements are claims that imply considerable underreporting in the Swedish cancer registry that allegedly would explain the lack of increase in glioma incidence. It has been shown that there is underreporting of *nervous system tumors* to the Swedish Cancer registry (Barlow et al., 2009), but the underreporting is mainly confined to the oldest age group (>70 years), where mobile phone use has not been very prevalent. Other examples are analyses of small geographical regions, where the random variation in the incidence rate from one year to another is considerable. By presenting data only for selected years and selected geographical regions, apparently high incidence rates can be reported.

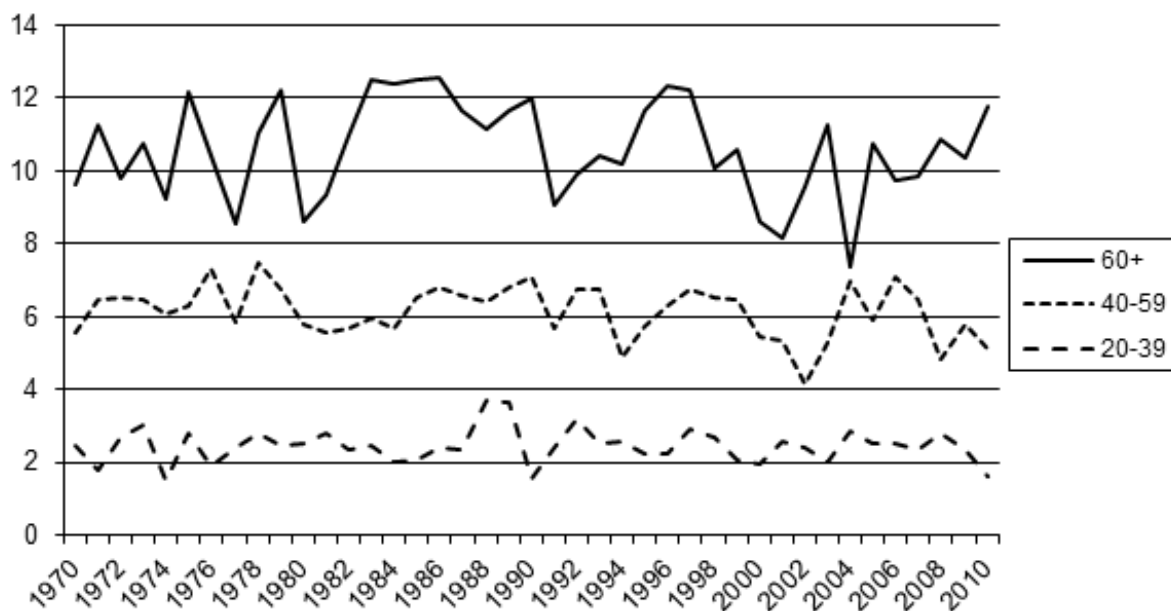
Overall, the incidence studies consistently report incidence trends for malignant brain tumors that are stable over time and not compatible with the reported risk increases in a few case-control studies.

Figure 3. Glioma incidence rates in Sweden 1970-2010. Age adjusted rate according to the world population per 100 000

a) men



b) women



WHAT DO WE KNOW TODAY?

Considerable amounts of epidemiologic data on mobile phone use and cancer risk have become available during the past 10 years. In parallel, the volume of experimental data on cells and animals has also increased substantially, see for example (Verschaeve et al., 2010).

Methodological limitations in the epidemiological studies have been identified and quantified. Recall bias is a problem in studies based on retrospective recall, especially in recall of amount of time spent on the phone and laterality of phone use. When evaluating the overall epidemiologic evidence one need to take into consideration how these potential sources of bias may affect results in studies of different designs.

The prevalence of mobile phone use has increased from a few percent to close to 100% in a few decades, which makes data on national cancer incidence trends highly informative.

The majority of epidemiological studies have found no evidence that mobile phone use is associated with an increased risk of glioma, meningioma, acoustic neuroma or other tumors. The few increased risk estimates observed were found in studies prone to recall bias, and the magnitude of the reported risk increases are such that they would definitely have resulted in a detectable increase in the brain tumor incidence rates if they were real. The cohort study, which is free from recall bias, found no increased risks, and the non-differential exposure misclassification would not be able to completely hide risk estimates of the magnitude reported in some of the case-control studies. In addition, the cohort findings are compatible with the observed incidence trends. The cohort study would probably not, however, be able to detect an increased risk in a very small subgroup of heavy users.

Discussion

Incidence studies from different parts of the world have consistently reported stable incidence rates for malignant brain tumors, e.g. glioma, and a very modest increase of acoustic neuroma. Brain tumor incidence rates in children and adolescents have also been stable since the introduction of mobile phones. Published incidence data are now available up to, and including, 2009.

Ten years ago there had already been a long period of research on health effects of electromagnetic fields, particularly on fields other than RF, such as fields that occur as a consequence of transmission, distribution, or use of electric power (ELF fields). Research on possible health effects from ELF fields was particularly intense during about two decades starting from the mid 80's. When the ELF research picked up speed little was known about dosimetry, techniques for measurements or detection of these fields or about distribution of exposure in the population. Therefore guidance in study design was rather limited in the beginning. Although the basic mechanism of interaction between these fields and humans was established long ago it was a somewhat open question whether other health effects existed than the ones anticipated based on this interaction mechanism. Some twenty years later a considerable amount of knowledge regarding many aspects of the ELF fields had accumulated. New meters suitable for large-scale assessment of individual exposure had been developed and they had also been used on large scale to collect data on exposure distributions in the population and in epidemiological studies looking at a variety of outcomes. The knowledge base had changed drastically and lots of information was then available about measurement techniques, and about results from epidemiological studies and other studies on health effects and on other biological effects.

This was about the same time as research into possible health effects of RF fields picked up speed and the situation was somewhat similar to the ELF situation

two decades earlier with respect to available knowledge. One essential difference was that the ELF research was motivated by an epidemiological study with results that gradually was confirmed in subsequent research (raised risk of leukemia in children), while for RF fields no such result existed and still does not exist. Since then and in particular during the last ten years our knowledge about RF fields has increased considerably: how they are absorbed in the human body, where they occur in the environment, and the likelihood of health risks.

With new mobile communication techniques and new usages the sources of RF exposure have increased substantially. At the same time, however, new and more energy efficient techniques have been introduced. One example is the switch from analogue to digital TV. It is therefore not obvious whether exposure levels in the population would have increased or decreased during this period. Systematic measurements in the environment are only available for the more recent time period and time trend data are uncertain.

Ten years ago, a number of studies, in particular double-blinded provocation studies, had found no evidence that ELF exposure was associated with occurrence of the symptoms that people who report themselves to be hypersensitive to electromagnetic fields refer to. During the last decade similar results have been obtained for RF fields.

A considerable number of studies on cancer, and in particular brain tumors, have now been presented. The data that have been collected in this research have also been used to look carefully at several methodological issues related to epidemiologic research on mobile phone use and brain tumor risk. As a consequence methodological data are now available that are very useful for the interpretation of this research. With a small number of exceptions the available results are negative and taken together with the methodological understandings the overall interpretation

is that these data provide no evidence for an association between mobile telephony and brain tumor risk. In addition, because mobile phone use has increased so rapidly over a short period of time, national cancer statistics are very useful sources of information. Had mobile phone use increased the risk of brain tumors it would have been visible as an increasing trend in the incidence rates in national statistics. But brain tumor rates are not increasing. Still one can never be absolutely certain and there is no data to evaluate latency periods exceeding, say, 15-20 years. For children there is still only one study available and this was negative, although with somewhat limited statistical power. So while there is no underlying reason to suspect that children would be at increased risk and while no research point in that direction, the database is still limited. Brain tumor incidence rates for children and adolescents have, however, also been stable since the introduction of mobile phones.

Two endpoints, “electromagnetic hypersensitivity” (a variety of acute, non-specific symptoms) and brain tumors have been at the forefront in the discussions about mobile communication and health risks. For neither of them has a biological hypothesis or initial study served as the starting point, but rather a general concern that some

information could have been overlooked regarding a new technology that spread very rapidly. In both instances, the data that have been accumulated do not speak in favor of increased risks. While absolute safety never exists, it seems increasingly unlikely that any of these endpoints is associated with RF field exposure. There is of course a huge range of other health outcomes that also could be investigated in relation to RF field exposure, but none for which there exists a credible hypothesis that calls for testing. Some observations have been made in the experimental research that warrants follow up. In particular neurophysiological research has found some EEG effects that merit a closer look.

The bottom line is that research on mobile telephony and health started without a biologically or epidemiologically based hypothesis about possible health risks. Extensive research for more than a decade has not detected anything new regarding interaction mechanisms between radiofrequency fields and the human body and has found no evidence for health risks below current exposure guidelines. While absolute certainty can never be achieved, nothing has appeared to suggest that the since long established interaction mechanism of heating would not suffice as basis for health protection.

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