Health Council of the Netherlands

Mobile phones and cancer

Part 3. Update and overall conclusions from epidemiological and animal studies

Gezondheidsraad
Health Council of the Netherlands

Aan de staatssecretaris van Infrastructuur en Milieu

Onderwerp : Aanbieding advies *Mobile phones and cancer. Part 3. Update and overall conclusions from epidemiological and animal studies*
Ons kenmerk : U-973760/EvR/pm/673-E3
Bijlagen : 1
Datum : 1 juni 2016

Geachte staatssecretaris,

Hierbij bied ik u het advies *Mobile phones and cancer. Part 3. Update and overall conclusions from epidemiological and animal studies* aan. Het advies is opgesteld door de Commissie Elektromagnetische velden en getoetst door de Beraadsgroep Volksgezondheid.

De commissie heeft systematische literatuurstudies uitgevoerd naar de epidemiologische en dierexperimentele gegevens over de relatie tussen blootstelling aan radiofrequente elektromagnetische velden en kanker. In het eerste advies, dat in juni 2013 is uitgebracht, zijn de epidemiologische gegevens besproken. Het tweede advies, gepubliceerd in september 2014, bevat de analyse van de dierexperimentele studies. In het voorliggende advies geeft de commissie een actualisering van de literatuur en integrale conclusies op grond van alle gegevens tezamen.

De commissie concludeert dat er geen bewezen verband is tussen langdurig en frequent gebruik van een mobiele telefoon en een verhoogd risico op tumoren in de hersenen of het hoofd-hals gebied. Een verband kan echter ook niet worden uitgesloten. Wel acht zij het onwaarschijnlijk dat blootstelling aan radiofrequente velden, die samenhangt met het gebruik van een mobiele telefoon, kanker veroorzaakt.

Ik onderschrijf de conclusies van de commissie.

Met vriendelijke groet,

prof. dr. W.A. van Gool,
voorzitter

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Gezondheidsraad
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To the State Secretary for Infrastructure and the Environment

Subject : Advisory report *Mobile phones and cancer. Part 2. Update and overall conclusions from epidemiological and animal studies*
Our reference : U-973824/EvR/pm/673-F3
Enclosure(s) : 1
Date : June 1st, 2014

Dear State Secretary,

I have the pleasure of presenting you the advisory report *Mobile phones and cancer. Part 3. Update and overall conclusions from epidemiological and animal studies*. It has been drafted by the Electromagnetic Fields Committee of the Health Council and reviewed by its Standing Committee on Public Health.

The Committee has performed systematic reviews of the epidemiological data and the data from animal experiments on the relation between exposure to radiofrequency electromagnetic fields and cancer. The first report, that was published in June 2013, discussed the epidemiological data. The second report, published in September 2014, contains the analysis of the studies on animal experiments. In the current report the Committee provides an update of the literature and overall conclusions based on the combined data.

The Committee concludes from this evidence that there is no established association between long-term and frequent use of a mobile telephone and an increased risk for tumors in the brain or head and neck. Such association can however also not be excluded. The Committee considers it unlikely that exposure to radiofrequency electromagnetic fields associated with the use of mobile phones, causes cancer.

I agree with the conclusions of the Committee.

Kind regards,
(signed)
Prof. dr. W.A. van Gool
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Mobile phones and cancer

Part 3. Update and overall conclusions from epidemiological and animal studies

to:

the State Secretary for Infrastructure and the Environment

the Minister of Economic Affairs

the Minister of Health, Welfare and Sport

No. 2016/06, The Hague, June 1st, 2016

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Samenvatting

Waarom dit advies?

De blootstelling aan radiofrequente elektromagnetische velden is in de afgelopen decennia aanzienlijk veranderd door de snelle groei van mobiele telecommunicatie, draadloos internet en andere bronnen. Dit heeft geleid tot groeiende bezorgdheid over mogelijke nadelige effecten van die blootstelling op de gezondheid. In 2012 heeft het International Agency for Research on Cancer (IARC) radiofrequente elektromagnetische velden geclassificeerd als 'mogelijk kankerverwekkend bij mensen'. Die classificatie is voornamelijk gebaseerd op gegevens uit epidemiologisch onderzoek, aangevuld met gegevens uit experimenten met proefdieren.

De commissie Elektromagnetische velden van de Gezondheidsraad heeft zowel de epidemiologische als de dierexperimentele gegevens systematisch geanalyseerd aan de hand van vooraf opgestelde protocollen en heeft daarbij ook de kwaliteit van de onderzoeken in aanmerking genomen. In 2013 kwam de commissie met haar analyse van de epidemiologische gegevens, en in 2014 met die van de dierexperimentele gegevens.[1,2] Het nu voorliggende advies geeft naast een actualisering van deze twee publicaties de in de eerdere adviezen aangekondigde eindconclusies van de commissie op grond van alle beschreven onderzoeksgegevens.

De commissie heeft gezocht naar epidemiologische gegevens over een mogelijke associatie tussen blootstelling aan radiofrequente velden van mobiele tele-

foons, en tumoren in de hersenen en andere weefsels in het hoofd en de nek (zoals hersenvliezen, gehoorzenuw en speekselklieren). Onderzoek naar andere bronnen van blootstelling aan radiofrequente velden en naar andere vormen van kanker wordt in dit advies niet behandeld. De onderzochte proefdierexperimenten hadden een bredere reikwijdte. Hierbij zijn alle mogelijke vormen van kanker onderzocht, evenals blootstelling aan alleen radiofrequente velden of in combinatie met kankerverwekkende stoffen.

Wat zijn de uitkomsten?

Uit de epidemiologische gegevens komen enkele zwakke aanwijzingen naar voren voor een verband tussen langdurig en intensief gebruik van een mobiele telefoon en een toename van het aantal gliomen (hersentumoren) en brughoektumoren (tumoren aan de gehoorzenuw). De bevindingen zijn biologisch soms niet plausibel. Zo zijn in enkele onderzoeken verhoogde risico's gevonden na een kortdurend gebruik, wat niet spoort met de lange groeitijd van de betreffende tumoren. In andere gevallen vond men bij de hoogste blootstellingniveaus geen toename van het aantal tumoren en bij lagere niveaus wel. Ook dat staat haaks op wat men zou verwachten. Verder bieden gegevens over het vóórkomen van de betrokken tumoren in Nederland en andere landen geen ondersteuning voor een oorzakelijk verband. Voor meningiomen (tumoren van de hersenvliezen), tumoren van de hypofyse en speekselkliertumoren zijn geen aanwijzingen gevonden voor een samenhang met het gebruik van mobiele telefoons.

De dierexperimentele gegevens leveren geen bewijzen dat blootstelling aan radiofrequente elektromagnetische velden tumoren kan opwekken. Mogelijk heeft een dergelijke blootstelling een effect op de verdere ontwikkeling van tumoren, maar de aanwijzingen daarvoor zijn zwak en in slechts één, heel specifiek, diermodel gevonden.

Wat zijn de conclusies?

De commissie heeft voor haar conclusies de epidemiologische en dierexperimentele bevindingen in samenhang beoordeeld. Naar haar oordeel kan niet worden gesteld dat er een bewezen verband is tussen langdurig en frequent gebruik van een mobiele telefoon en een verhoogd risico op tumoren in de hersenen of het hoofd-hals gebied. Op basis van de zeggingskracht van de beschikbare gegevens kan volgens de commissie slechts worden geconcludeerd dat zo'n verband niet valt uit te sluiten. De commissie acht het onwaarschijnlijk dat blootstelling aan

radiofrequente velden, die samenhangt met het gebruik van een mobiele telefoon, kanker veroorzaakt. Gegevens uit dierexperimenten wijzen op de mogelijkheid dat blootstelling aan dergelijke velden de ontwikkeling van tumoren stimuleert. Het is echter onduidelijk of hiermee de toegenomen kans op tumoren in de hersenen en het hoofd-halsgebied, die in sommige epidemiologische onderzoeken is waargenomen, kan worden verklaard. De commissie vindt het waarschijnlijker dat een combinatie van verstoring, vertekening en toeval de verklaring vormt voor de epidemiologische bevindingen.

Is er aanleiding om de blootstelling te verminderen?

Uit de zojuist geformuleerde conclusies vloeit voort dat onduidelijk is welke waarde maatregelen hebben om de blootstelling aan radiofrequente elektromagnetische velden te verminderen. Toch wil de commissie haar eerdere aanbeveling herhalen: pas het ALARA-principe toe. Dat wil zeggen: houd de blootstelling zo laag als redelijkerwijs mogelijk is (*As Low As Reasonably Achievable*). Het is bijvoorbeeld onnodig dat apparatuur met een groter vermogen of gedurende een langere tijdsperiode uitzendt dan noodzakelijk is om een goede verbinding te hebben. De commissie stelt zich hiermee achter de aanbevelingen uit het advies *Voorzorg met rede* van de Gezondheidsraad.[3]

Blijft er onderzoek nodig?

Er zijn nog steeds heel weinig gegevens over langetermijneffecten bij mensen. Weliswaar zijn in sommige epidemiologische onderzoeken termijnen van dertien jaar of langer onderzocht, maar over het algemeen werden slechts weinig personen zo langdurig gevolgd. De latentietijden voor de ontwikkeling van de relevante tumoren zijn hoogstwaarschijnlijk langer. De commissie vindt het daarom belangrijk dat de lopende cohortonderzoeken waarin de gezondheidseffecten van het gebruik van mobiele telefoons worden onderzocht, door blijven gaan. Deze onderzoeken zullen meer gegevens opleveren, waardoor met meer zekerheid conclusies getrokken kunnen worden. De bepaling van de blootstelling is in alle beschikbare onderzoeken erg zwak. Het is daarom van het grootste belang dat in lopende en toekomstige onderzoeken de blootstelling aan radiofrequente velden nauwkeuriger en objectiever wordt bepaald. Dit is des te meer van belang omdat de blootstelling aan radiofrequente velden voortdurend verandert door veranderingen in het gebruik en de ontwikkeling van nieuwe mobiele telecommunicatiemiddelen.

Summary

Why this report?

Exposure to radiofrequency electromagnetic fields has considerably changed in the past decades, due to the fast growth of mobile telecommunication, wireless internet access and other sources. This has increased concern about possible adverse health effects of such exposures. In 2012, the International Agency for Research on Cancer (IARC) classified radiofrequency electromagnetic fields as 'possibly carcinogenic to humans'. This classification was primarily based on epidemiological data, with additional support from animal studies.

The Electromagnetic Fields Committee of the Health Council of the Netherlands has performed systematic reviews of both the epidemiological and animal experimental data using *a priori* defined protocols, taking into account the scientific quality of the studies. The analysis of the epidemiological data has been published in a report issued in 2013.[1] The analysis of the data on carcinogenesis in experimental animals was published in 2014.[2] This report provides an update of the two previous reports and the overall conclusions of the Committee on the basis of all described data that was announced in the previous reports.

Epidemiological evidence was sought for indications of an association between exposure to radiofrequency fields from mobile phones and tumours in the brain and various other tissues in the head and neck (e.g. meninges, acoustic nerve, parotid glands). Studies investigating other sources of exposure to radiofrequency fields and other cancers are not discussed in this report. The animal carcinogenesis studies had a broader scope and included all possible cancers, as well as exposure to radiofrequency fields alone and co-exposures to carcinogenic agents.

What has been observed?

Overall, the epidemiological data show some weak indications for an association between prolonged and intensive use of a mobile phone and an increased incidence of gliomas (brain tumours) and acoustic neuromas (tumours on the acoustic nerve). In some cases these findings lack biological plausibility. Some studies showed for instance increased risks after a short period of use, which is not compatible with the long period of development of the tumours in question. In other studies an increase in the number of tumours was not observed with the highest exposure level, but only with lower ones. This is also in contrast to expectations. Furthermore, data on the incidence of the relevant tumours from the Netherlands and other countries worldwide do not provide support for a causal relationship. For meningiomas, pituitary tumours and parotid gland tumours, no indications for an association with mobile phone use have been observed.

The animal studies do not provide evidence for induction of tumours by exposure to radiofrequency electromagnetic fields. Such exposure may have a promoting effect on the development of tumours, but the indications for this are weak and have been observed in only one, very specific, animal model.

What are the overall conclusions?

The Committee jointly considered the epidemiological and experimental data to formulate its conclusions. The Committee feels that it is not possible to state that there is a proven association between long-term and frequent use of a mobile telephone and an increase in the risk of tumours in the brain and head and neck region in humans. Based on the strength of the evidence it can only be concluded that such an association cannot be excluded. The Committee considers it unlikely that exposure to radiofrequency fields, which is associated with the use of mobile

telephones, causes cancer. The animal data indicate a possibility of a promoting effect, but it is not clear whether this could explain the increased risk for tumours in the brain, head and neck that has been observed in some epidemiological studies. The Committee feels it more likely that a combination of bias, confounding and chance might be an explanation for the epidemiological observations.

Is there reason to limit exposure?

From the conclusions formulated above it follows that the value of any measures to reduce exposure is unclear. Nevertheless, the Committee would like to repeat its previous suggestion: apply the ALARA principle. This means that exposures should be As Low As Reasonably Achievable. There is, for instance, no need for any device to transmit with greater power or for a longer period of time than needed for an adequate connection. This is fully in line with the suggestions from the Health Council's advisory report *Prudent precaution*.[3]

Is more research necessary?

There is still very limited information on really long-term effects in humans. Some epidemiological studies have follow-up times of more than 13 years, but with generally few subjects in the highest exposure categories. The latency times for development of the relevant tumours are most likely longer. The Committee therefore considers it important to continue the ongoing cohort studies evaluating the health effects of mobile phone use, in order to provide more conclusive human evidence. The exposure characterization in all currently available studies is very poor. It is therefore very important that ongoing and future studies incorporate more accurate and objective assessment of RF exposure. This is even more important since personal exposure to RF continues to change due to evolving patterns of use and new mobile telecommunication devices.

Chapter 1

Introduction

1.1 Background

The fast and extensive growth of mobile telephony and the resulting increase in exposure of people to radiofrequency electromagnetic fields (RF EMF) has increased concern for adverse effects resulting from such exposure. Especially dreaded are possible effects on the induction or promotion of the growth of cancer. Many studies have been published in the past decades, and on the basis of the available results the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) has classified RF EMF in 2010 as 'possibly carcinogenic to humans' (class 2B).[4] This classification was primarily based on the results of epidemiological studies on the relation between mobile phone use and the risk of glioma (tumours of brain tissue) and acoustic neuroma (tumours of the acoustic nerve sheath), and on some data from experimental studies with animals which relate longterm exposure to tumour incidence.[5]

The Electromagnetic Fields Committee of the Health Council of the Netherland (designated further in this report as 'the Committee') has performed its own, independent, systematic reviews of the literature on this subject. In a first report it has described the epidemiological data[1], while a second report discussed the outcomes of experimental animal studies.[2] In both reports, data collection, extraction and analysis have been done in a predetermined systematic way. The

composition of the Committee at the time of writing of the current report is given in Annex A.

1.2 The research question

The basic question the Committee investigates in these reports is, whether there are indications for a causal relationship between exposure to RF EMF from mobile phones and tumours in the brain and various other tissues in the head (e.g. meninges, acoustic nerve, parotid glands). To this end, the Committee has performed systematic analyses of the relevant epidemiological and animal experimental literature.

The Committee has focussed on exposure to RF EMF by the use of mobile phones, since this is the only type of exposure for which in some studies positive associations with an increase in incidence in tumours in the head and neck region have been observed. In other studies other types of exposure have been investigated (e.g. exposures from sources in the living or work environment, such as mobile telephone masts) in which also cancer in other parts of the body has been studied. These studies have not shown any association with factors indicative of exposure (such as distance to the source) and an increased risk of cancer, and are not discussed in this report.

1.3 Exposure

In general, it is virtually impossible to assess with reasonable confidence what the exposure to RF EMF from mobile phones or other sources has been in the past. This is the case for exposures in the recent past, and even more for exposures several years ago. The same is true for assessment of the intensity and duration of use of a mobile phone, that has in most epidemiological studies been used as a proxy for exposure. So inherently the exposure assessment in retrospective studies such as case-control and case-case studies and retrospective cohort studies is poor. The only type of study that may have a better exposure assessment is a prospective cohort study, since that may include actual exposure assessment at different time periods during the follow-up.

Assessment of the exposure to RF EMF resulting from the use of mobile phones is also hampered by the continuing technical developments that result in new, improved, types of phones that use different types of signals than their predecessors. These newer phones also often lead to the changes in their use. For

instance, the use of smartphones has changed the way of using a phone from primarily making calls to more text- and app-related use. This also leads to changes in exposure, since the phones are not held against the head so much anymore.

In several epidemiological studies discussed in this and in the previous report, different phone types are distinguished. The oldest type is the analogue phone, that generally used simple modulation of a carrier frequency to transmit speech and text information. This was succeeded by the digital GSM phone, that used a pulse modulation of the carrier frequency for speech, text and data transmission. The next, 3rd, generation of mobile phones was UMTS, using yet another, more complex, type of signal to allow in particular more and faster data transfer. With increasing demand, the capabilities of UMTS would not suffice, therefore a 4th generation type of mobile phone system has been developed and the 5th generation is underway. Another type of wireless phone that is nowadays in use in most households is the cordless phone (mostly using the DECT protocol). This is a phone with a limited range that is connected through a small base station to the landline network and that replaces as such the old wired phones. In the report *Mobile telephones* the Committee has provided detailed technical information on the different generations of mobile phone and DECT systems.[6]

Exposure from other sources, such as tablets, laptops and WiFi systems, is complex and different from that of mobile phones. In any case such sources do not result in appreciable exposure of the head.

1.4 Causation

Associations observed in epidemiological studies may be indicative for a causal relationship, but in general it is difficult to establish a causal relationship from epidemiological evidence only, unless the association is consistently observed and the risk observed is high. Observing a dose-response relationship, i.e. an increase of the risk with increasing dose, is also an indication for a causal association. However, it is questionable whether the concept of 'dose', which is the product of the level and duration of exposure, can be applied to exposure to electromagnetic fields. In a short advisory report on power lines from 2008, the Committee indicated that there are no indications that 'dose' can be applied to low-frequency fields.[7] The same can be concluded for radiofrequency fields. It is simply not known whether there is more damage inflicted by higher exposure levels and whether there is accumulation of damage with longer exposure. In

combination with the problems associated with assessing the exposure in epidemiological studies, this makes the concept of 'dose' impossible to use. Therefore, and for simplicity, the Committee uses in this report the term 'exposure-response relationship', which may refer to an exposure level-response relationship or an exposure duration-response relationship.

When analyzing epidemiological data, it is important to take into account a number of considerations formulated by Bradford Hill, in order to conclude on the possibility of a causal relationship.[8] These include strength, consistency, temporality, biological gradient (or exposure-response) and plausibility. The Committee wil discuss them in the final chapter of this report.

1.5 This report

In the current report the results of the two previous reports are updated, summarized and integrated.

The report starts in Chapter 2 with an update of the epidemiological data: results are presented of the systematic search and analysis of the epidemiological studies that have been published since the closing date of the first report of the Committee[1] and an updated overview is provided of studies investigating the incidence of various types of tumours in the head and neck over time. Following an a priori defined protocol, all relevant studies, both case-control, cohort and other types of studies, were identified, extracted, selected for further analysis and evaluated for their quality. In addition, the Committee provides in this chapter an update of the data on the incidence of gliomas and parotid gland tumours in the Netherlands, using 10-year age classes and data up to 2012.

Chapter 3 presents the results of a systematic search and analysis of the experimental animal studies that have been published since the closing date of the second report of the Committee.[2]

In Chapter 4 the Committee discusses the evidence from the epidemiological and experimental data and gives its overall conclusions.

Chapter 2

Recent epidemiological data

2.1 Search and selection

Since the publication of the report of the Committee on the systematic analysis of the epidemiological data, several new studies and re-analyses of older studies have been published. On May 29, 2015, a additional systematic search in PubMed was performed, updating the last search done on August 14, 2011, with the following search protocol:

((cellular phone* OR mobile phone* OR cell phone* OR radio waves OR electromagnetic fields OR radio frequency) AND (tumour* OR cancer* OR neoplasm*) AND (epidemiology OR case-control OR cohort OR case-case OR dosimetry OR exposure assessment) AND ("2011/08/15"[Date - Entrez]: '3000'[Date - Entrez])) NOT (animal* OR rat OR rats OR mouse OR mice OR in vitro)

This resulted in 451 hits. A first inspection on the basis of the titles resulted in 89 papers that could potentially be used. Of the excluded 362 papers, 188 were not on tumours in the head, 80 were on treatment, 29 were on extremely low frequency fields, 10 were on animal or in vitro studies, 3 were on calculations of exposure, 3 were on radio-, tv- or GSM masts, and 49 were on other topics.

The 89 selected papers were further inspected on the basis of the abstract or full text. This resulted in 10 papers that were to be fully analysed. Of the excluded 79 papers, 21 were editorials or correspondence, 20 were reviews, 7 were not on

mobile phones, 4 were not on tumours in the head, 5 were ecological studies, 5 had already been described in the previous report, 1 was a pooled analysis of studies described in the previous report, 2 were on the association between mobile phones and the survival of cancer patients, 4 were on therapy, 1 was on technical issues, 4 were on theoretical issues, and 5 were in languages other than English, French, German or Dutch.

The 10 remaining studies have been systematically evaluated in the same way as the studies in the first report of the Committee.[1]

2.2 Quality analysis of cohort, case-control and case-case studies

In the previous report[1], the Committee has developed a system to score the quality of epidemiological studies. In Annex B this is discussed in more detail. In the following tables, the overall score of the quality analysis is provided as a number between 0 and 10. To facilitate distinguishing higher from lower rated studies, they are colour coded, but without any particular meaning of the cut-off values. Ratings of 7.0 and higher are marked green, ratings of between 3.0 and 7.0 are marked yellow, and ratings lower than 3.0 are marked red. In order to provide a complete overview of the quality of all identified epidemiological studies, the newly identified studies are added to the information from the studies presented in the previous report.[1]

2.2.1 Cohort studies

One new cohort study has been published recently. The study population is a cohort of about 800,000 middle-aged women who are surveyed every 3-4 years on sociodemographic, medical and lifestyle factors. In the 1999-2005 survey, a general question about mobile phone use was included. The description of the study is given in Table 1, the results are given in Annex D.

Table 1 Cohort studies.

Reference	Type of tumour	Exposure assessment	Country / time period / ages	Overall score (0-10)
Studies from previous report				
Dreyer et al. (1999)[9]	Brain cancer	Length contract, type phone, duration calls	Boston, Chicago, Dallas, Washington DC, USA, 1994 ≥ 20 y at start	7.1
Frei et al. (2011)[10]	Brain tumours, including glioma, meningioma	Length of contract for those with contract before 1996	Denmark, 1982-2007 ≥ 30 y at start	7.9
Schüz et al. (2011)[11]	Acoustic neuroma	Length of contract for those with contract before 1996	Denmark, 1982-2006 ≥ 30 y at start	7.9
New study				
Benson et al. (2013)[12]	Brain tumours combined, glioma, meningioma, acoustic neuroma	One-time question on mobile phone use: never, less than once a day and every day	UK, 1996-2001, women mean age 59.5 y	7.8

Abbreviations: CI: confidence interval; IRR: incidence rate ratio; OR: odds ratio; SMR: standard mortality rate.

2.2.2 Case-control studies

These include 4 new studies from the Hardell group and 5 new studies from other research groups. The studies from the Hardell group are presented separate from the other studies since they form a large cluster of often overlapping studies. Presenting them in a separate table provides a better overview. The description of the studies is given in Tables 2 and 3, the results are given in Annex D.

Table 2 Case-control studies of the Hardell group.

Reference	Type of tumour	Original, pooled / study no.	Population, hospital based / ages	Response (%)	Time period / place	Overall score (0-10)
Studies from previous report						
Hardell et al. (2009)[13]	Brain tumour (incl. glioma, meningioma, acoustic neuroma)	Pooled, studies nrs 2+3	Population 20-80 y	Cases: 90% (malignant tum.); 88% (benign tum., incl. meningioma, acoustic neuroma) Controls: 89%	1997-2003 Study 2: central region Sweden, study 3: 2 city regions Sweden	7.4
Hardell et al. (2011)[14]	Malignant brain tumour	Pooled, studies nrs 2+3+4	Population 20-80 y	Cases: 85% Controls: 84%	1997-2003 Study 2: central region Sweden, study 3: 2 city regions Sweden; study 4: 4 city regions Sweden	7.4

Hardell et al. (2004)[15]	Parotid gland tumour	Original	Population 20-80 y	Cases: 64%[a] Controls: 90%[a]	1994-2000 6 city regions Sweden	6.4
Söderqvist et al. (2012) [16]	Parotid gland tumour	Original	Population 22-80 y	Cases: 75%[a] Controls: 83%	2000-2003 3 city regions (9/ 21 counties) Sweden	7.2
New studies						
Hardell et al. (2013)[17]	Malignant brain tumours	Original (study nr 5)	Population 18-75 y	Cases: 87% Controls: 85%	2007-2009 6 Swedish cancer registries	7.4
Hardell & Carlberg (2015)[18]	Glioma	Pooled, studies nrs 2-5	Population 20-80, 18-75 y	Cases: 89% Controls: 87%	1997-2003, 2007-2009 Study 2: central region Sweden, study 3: 2 city regions Sweden; study 4: 4 city regions Sweden, study 5: 6 Swedish cancer registries	7.4
Hardell et al. (2013) [19]	Acoustic neuroma	Pooled, studies nrs 2+5 (acoustic neuroma data from study nr 5 not published separately)	Population 20-80, 18-75 y	Cases: 93% Controls: 87%	1997-2003, 2007-2009 Study 2: central region Sweden, study 5: 6 Swedish cancer registries	7.9
Carlberg et al. (2013) [20]	Meningioma	Original	Population 18-75 y	Cases: 88% Controls: 85%	2007-2009Cancer registries, all of Sweden	7.4

[a] Recalculated by including excluded cases that were deceased or declared too ill by their physician. This was only done for the studies where these subpopulations had been included in the response calculations. See the previous report.[1]

Table 3 Case-control studies from research groups other than Hardell.

Reference	Type of tumour	Original, pooled	Population, hospital based / ages	Response (%)	Time period / place	Overall score (0-10)
Brain tumours, gliomas						
Studies from previous report						
Takebayashi et al. (2008)[21]	Glioma, meningioma, pituitary adenoma	Original	Hospital for cases estimated to represent 75% of total # of cases in area, population controls 30-69 y	Cases: glioma 59%, meningioma 78%, pituitary adenoma, 76% Controls: 51%	2000-2004 Greater Tokyo area, Japan	5.5
INTERPHONE study group (2010)[22]	Glioma, meningioma	Pooled	Mixed 30-59 y	Cases: glioma 64% (36-92%), meningioma 78% (56-92%) Controls: 53% (42-74%)	2000-2004 13 countries	6.6
Muscat et al. (2000)[23 a]	Primary brain cancer, incl. glioma	Original	Hospital 18-80 y	Cases: 82% Controls: 90%	1994-1998 New York, Providence, Boston, USA	3.9
Inskip et al. (2001)[24]	Glioma, meningioma, acoustic neuroma	Original	Hospital ≥ 18 y	Cases: 92% Controls: 86%	1994-1998 Phoenix, Boston, Pittsburgh, USA	5.0
Auvinen et al. (2002)[25]	Glioma, meningioma, parotid gland tumour	Original	Population 20-69 y	Cases: 100% Controls: 100% as register-based	1996 All of Finland	8.4
Gousias et al. (2009)[26]	Glioma	Original	Population 22-82 y	Cases: 100%? Controls: 100%?	2005-2007 6 districts of Greece	2.1
Baldi et al. (2011)[27]	Brain tumours	Original	Population ≥ 15 y	Cases: 70% Controls: 69%	1999-2001 Gironde, France	5.7
Aydin et al. (2011)[28]	Brain tumours children	Original	Population 7-19 y	Cases: 83% Controls: 71%	2004-2008 All of Denmark, Sweden, Norway, Switzerland	7.5
Spinelli et al. (2010)[29]	Glioma	Original	Hospital ≥ 18 y	Cases: 72% Controls: 100%?	2005 Marseille, Toulon, France	2.7
New studies						
Coureau et al. (2014) [30]	Glioma, meningioma	Original	Population ≥ 16 y	Cases: 73% Controls: 45%	2004-2006 4 regions in France	5.8

Feltbower et al. (2014) [31]	Brain tumours	Original	Hospital 0-24 y	Cases: 71 % Controls: 74 %	2007-2009 (Leeds); 2008-2010 (Manchester) 2 hospitals in Leeds and Manchester (pilot study)	2.2
Acoustic neuroma						
Studies from previous report						
INTERPHONE study group (2011)[32]	Acoustic neuroma	Pooled	Mixed 30-59 y	Cases: 82% (70-100%) Controls: 53% (35-74%)	2000-2004 13 countries	7.1
Muscat et al. (2002)[33]	Acoustic neuroma	Original	Hospital ≥ 18 y	Cases: 100%? Controls: 100%?	1997-1999 New York, USA	3.4
New studies						
Corona et al. (2012)[34]	Acoustic neuroma	Original	Hospital ≥ 18 y	Cases: 88 % Controls: 83 %	2006-2010 2 municipalities in northeast Brazil	3.8
Moon et al. (2014)[35]	Acoustic neuroma	Original	Hospital ≥ 18 y	Cases: 89% Controls: not provided	1991-2010 One hospital in Seoul, South Korea	3.9
Pettersson et al. (2014) [36]	Acoustic neuroma	Original	Population 20-69 y	Cases: 83% Controls: 65%	2002-2007 Swedish regional cancer registers; local acoustic neuroma registries at otorhinolaryngology clinics in Uppsala and Linköping regions	7.2
Parotid gland tumour						
Studies from previous report						
Duan et al. (2011)[37]	Parotid gland tumour	Original	Hospital 7-80 y	Cases: 78% Controls: 62%	1993-2010 Beijing, China	4.3
Lönn et al. (2006)[38 b]	Parotid gland tumour	Original	Population 20-69 y	Cases: 85% overall (79% Denmark, 89% Sweden) Controls:70% overall (60% Denmark, 72% Sweden)	2000-2002 All of Denmark, 3 cities Sweden	6.5
Sadetzki et al. (2008)[39]	Parotid gland tumour	Original	Population ≥ 18 y	Cases: 87% Controls: 66%	2001-2003 All of Israel	6.4

Other tumours

Studies from previous report						
Stang et al. (2001)[40]	Uveal melanoma	Original	Population 35-69 y + Hospital 35-74 y	Cases: 84% Controls: 81%	1994-1997 Essen+ all of Germany	4.6
Stang et al. (2009)[41]	Uveal melanoma	Original	Hospital 20-74 y	Cases: 94% Controls: 57% (hospital) & 52% (population)	2002-2004 Essen, Germany	7.5
Warren et al. (2003)[42]	Intratemporal facial nerve tumours	Original	Hospital Cases: mean 47 y Controls: mean 57.8, 52.6, 50.8 y	Cases: 100%? Controls: 100%?	1995-2000 Gainesville (Fl), USA	2.0
Schoemaker et al. (2009)[43]	Pituitary tumours	Original	Population for cases, general physicians for controls 18-59 y	Cases: 61% (calculated) Controls 43%:	2001-2005 South-east UK	7.1
De Roos et al. (2001)[44]	Neuroblastoma	Original	Hospital ≤ 19 y	Cases: 73% Controls: 71%	1992-1994 139 hospitals, USA & Canada	0.8

2.2.3 Case-case studies

One new paper included both a case-control and a case-case study (Moon et al., 2014).[35] The case-control study was described in the previous paragraph, the case-case study is described here. The results are given in Annex D.

Table 4 Case-case studies.

Reference	Type of tumour	Original, pooled	Population, hospital based / ages	Response (%)	Time period / place/ topic of analysis	Overall score (0-10)
Studies from previous report						
Ali Kahn et al. (2003)[45]	Glioma	Original	Hospital 20-81 y	100%	2000-2001 One hospital in Dublin, Ireland Handedness in phone users vs. tumour location	6.0
Salahaldin & Bener (2006)[46]	Acoustic neuroma	Original	Hospital 34-66 y	100%?	2004-2005 Two hospitals in Doha, Qatar Possession of phone (yes / no)	5.2

Sato et al. (2010)[47]	Acoustic neuroma	Original	Hospital ≥29 - ≤70 y	51%	2000-2006 22 hospitals in Japan Intensity of phone use and laterality vs. tumour location and size	8.3
New study						
Moon et al. (2014)[35]	Acoustic neuroma	Original	Hospital ≥ 18 y	Cases: 100%	1991-2010 One hospital in Seoul, South Korea Association of tumour volume with mobile phone use	7.5

2.2.4 *Conclusions on the quality analysis*

Most of the new studies described here are of an adequate quality according to the grading system used. The pilot study of Feltbower et al.[31] scored low on the methodological quality criteria "selection bias" and "misclassification of exposure" (see Table B5 in Annex B). The case-control studies of Corona et al.[34] and Moon et al.[35] scored low on the criteria "selection bias" and "correction for confounding" (see Table B5 in Annex B).

The grading system used is adequate for describing the general quality of the design and execution of the individual studies. In the previous report, however, the Committee already argued that, since it does not compare the studies, it does not capture any internal inconsistencies between studies from the same investigators.[1] Such inconsistencies can be identified for the Hardell studies. In the previous report, the Committee mentioned that a striking feature of the Hardell case-control studies is their generally high response rate. In several of the studies from other groups discussed in the current report, similar high response rates have been obtained as in the more recent Hardell studies. Therefore the Committee does not consider the response rates in these recent Hardell studies as unrealistically high. However, the other critique to the Hardell studies is still valid. The authors have conducted a limited number of primary studies, but they combine their results in different ways in the various pooled analyses. They consider a large number of endpoints, which often vary between studies and pooled analyses, without clearly defined *a priori* hypotheses on endpoints or cut-off points for the exposure metrics (see tables D1-8 and D10-13 in Annex D). There are often inconsistencies between endpoints. Also, increased risks are

sometimes found already for very short follow-up times, such as >1-5 years. This is unlikely in view of the long latency times assumed for the types of tumours involved. Another issue is, that often an exposure-effect relationship is not present, although this in part may be the result of low numbers of subjects in the higher exposure categories. Because of these issues, the Committee has given the Hardell studies less weight in the overall analysis than would be the case on the basis of the results of the grading system as such.

2.3 Results of the new cohort, case-control and case-case studies

The results of the newly identified studies are presented in tables D1-14 in Annex D and are briefly described here.

2.3.1 Cohort study

In the million-women study by Benson et al. (2013)[12] an increased risk was observed for acoustic neuroma associated with ≥ 10 years use of a mobile phone (relative risk = 2.46, 95% confidence interval 1.07, 5.64 (Table D5)). No increased risks were found for glioma (Table D1), meningioma (Table D10) and pituitary tumour (Table D14), nor with other exposure metrics (ever or daily use of a mobile phone) or for other tumours (results not presented).

2.3.2 Case-control and case-case studies

Glioma

Hardell et al. (2013)[17] performed a new study into the relationship between mobile phone use and malignant brain tumours. The results were subsequently included in a new pooled analysis of these data that included the data from three previous studies.[18] This pooled analysis showed increased risks for time since first use of generally more than 5 years for various types of mobile phones (analogue, GSM and UMTS) separately and combined, and for cordless phones for time since first use of more than 1 year (Table D1). For cumulative call time, increased risks were found for analogue phones for 123 or more hours, for GSM for more than 1 hour and for UMTS for 512-1,486 hours (Table D2). For all types of mobile phones combined, increased risks were found for cumulative call times of more than 1 hour. For cordless phones, increased risk was found for call times of more than 512 hours. When the data were analysed for laterality,

increased risks were found for ipsilateral use* for ever use of any type of phone except UMTS (Table D3) and for time since first use of more than 1 year. For all mobile phones combined, increased risk was also found for contralateral use of more the 20 years. When analysed as continuous variables, the risk was increased per 100 hours of use and per year of use for analogue and GSM phones, all mobile phones combined, and cordless phones, but not for UMTS phones (Table D4).

Acoustic neuroma

Hardell et al. (2013)[19] published the pooled results for acoustic neuroma of a previous study and a new one (the data from the latter one were not published separately). For analogue phones they observed increased risks for all categories of time since first use of more than 1 year, and for GSM for more than 1 year, or more than 5 to 10 years (Table D5). For all mobile phones combined increased risks were observed for all times since first use of more than 1 year. For cordless phones risks were increased for time since first use of more than 1 year, and for more than 1 to 5 and more than 5 to 10 years.

In a study by Corona et al. (2012)[34] no increased risks were observed for times since first use of up to more than 6 years (Table D5). Moon et al. (2014)[35] also did not observe increased risks for acoustic neuroma with average times since first use of around 10 years, while Petterson et al. (2014)[36] found only an increased risk for digital or cordless phones used for 5-9 years, but not for longer or shorter periods; for analogue and digital phones combined they did not observe increased risks.

For cumulative call time, Hardell et al. (2013)[19] found increased risks for analogue phone use with all call times of more than 1 hour, and the same for GSM phones, except for call times of 123-155 hour (Table D6). A similar pattern was observed for all mobile phones combined. Cordless phone use showed an increased risk for call times more than 122 hour.

Moon et al. (2014)[35] found no difference between cases and controls with respect to cumulative call times. Pettersson et al. (2014)[36] found an association between cumulative call time and risk for acoustic neuroma for cordless phones, but when considering only the histologically confirmed cases the results were less apparent

* Use of the phone predominantly on the same side of the head as where the tumour is located.

and they conclude that it is unlikely that there is a causal relation between the reported exposure and acoustic neuroma formation.

When the data were analysed for laterality, Hardell et al. (2013)[19] found increased risks for both ipsi- and contralateral use with ever use of an analogue phone, and with ipsilateral use of a GSM, but not of a UMTS phone, with all mobile phones combined, and with use of a cordless phone (Table D7). Corona et al. (2012)[34] and Pettersson et al. (2014)[36] did not find any increased risk for either ipsi- or contralateral use with any endpoint considered. The latter authors also conclude that their data show that laterality analyses are prone to bias and that their results suggest that detection bias may be present in studies of a slow-growing tumour such as acoustic neuroma.

When analysed as continuous variables by Hardell et al. (2013)[19], the risk was increased per 100 hours of use and per year of use for analogue phones, all mobile, digital or wireless phones combined, but not for GSM, UMTS and cordless phones separately (Table D8). An increase in tumour volume was found for analogue phones only per 100 hours of use and per year of use. In a case-case study that was included in the publication by Moon et al. (2014)[35] a larger tumour volume was observed for those with regular use of a mobile phone, and, in the group of regular users, for those who used their phone for more than 20 min per day and for those with a cumulative use of more than 2,000 hour (Table D9).

Meningioma

No increased risks were observed for meningioma by the Hardell group in a study by Carlberg et al. (2013)[20] for time since first use (Table D10) and cumulative call time (Table D11). No effect of laterality was observed for ever use of any type of phone (Table D12). However, increased risks were found for all phone types except UMTS per 100 hour of use, but not per year of use (Table D13). Also no effects of these variables were found for changes in tumour volume.

2.3.3 *Conclusions on the cohort, case-control and case-case studies*

Some epidemiological studies provide indications for an association between long-term or intensive use of a mobile telephone and an increased risk of tumours in the brain or head and neck region. However, the studies are not consistent and of varying quality. Increased risks have sometimes been observed with short time periods of use, which is unlikely in view of the slow growing nature of the

tumours involved. And in some cases increased risks have been observed only in an intermediate category of exposure, but not in higher ones. This is contrasting the expectation of an increased response with increasing exposure. The final conclusion is, that overall the evidence for an association is weak.

2.4 Ecological studies

These studies investigate the occurrence of disease at population level in relation to the prevalence of (a proxy for) exposure in the population. They may analyze for instance the pattern of tumour occurrence over time (either by incidence or by mortality) in geographic entities such as countries, to identify any trends and to see whether these could be explained e.g. by trends in possession or use of mobile phones. Individual data on mobile phone use are not used in these studies. Such studies will inherently be limited by the poor level of insight into trends and patterns of mobile phone use, and hence of actual exposure, particularly for specific age, sex and other population group definitions.

It should be noted that for many countries substantial and wide-spread mobile phone use is relatively recent (Figure 1).

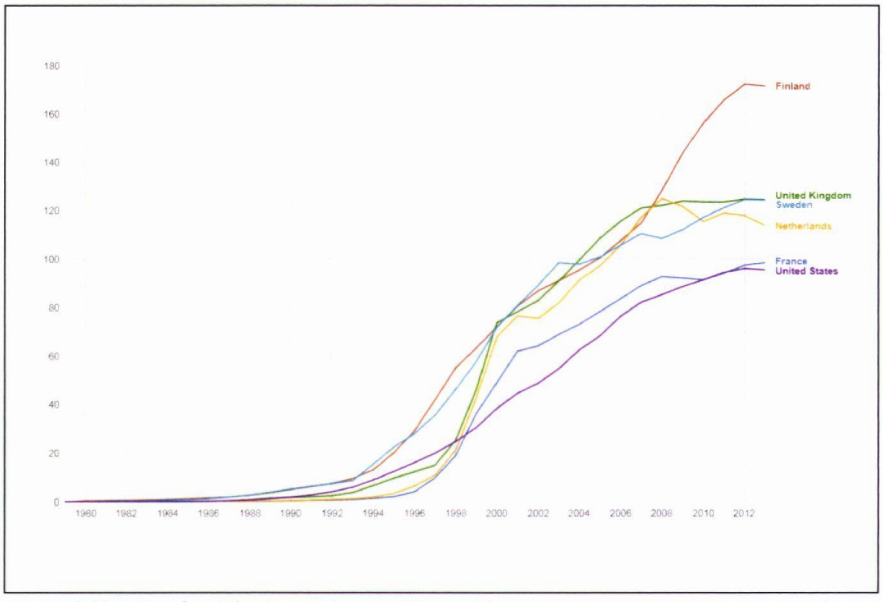

Figure 1 Number of mobile phone subscriptions per 100 inhabitants for some European countries and the USA. Data from ITU (http://www.itu.int/ITU-D/ict/statistics/explorer/index.html).

In most Western-European countries approximately half of the population had a mobile phone subscription in the year 2000. In the Nordic countries (Norway, Sweden, Finland and Denmark) the increase started earlier, but was caught up by the other countries around the century mark. By 2005 most people in the countries presented (except France and the USA) owned a mobile phone, but the extent of use is much less certain.

The studies selected from the search mentioned in the previous paragraph included 5 ecological studies (studies on time trends of incidence of the respective tumours). However, a separate search was made using broader search terms into ecological studies investigating time trends of tumours in the head. This resulted in 23 studies, which are summarized in Table C1 in Annex C. These studies have not been evaluated in a similar systematic way as the case-control and cohort studies; instead, a description of the studies and their main findings are provided. A distinction is made between studies that include a time period up to 2005 and later. The latter ones are considered more relevant for any relationship between tumour incidence and mobile phone use, since massive phone use did not start until the mid-1990's and most tumours presumably have a long latency time of at least 10 years, as described in the previous report.[1] (The Committee acknowledges, however, that this is an assumption with a considerable degree of uncertainty.) It is thus possible that any trends in tumour occurrence related to mobile phone use may not yet be visible in most countries, with an exception perhaps for the Nordic countries, since use started earlier there.

In analyzing ecological studies, it has to be realized that trends in mortality can also be influenced by the introduction of more effective treatments and that trends in incidence can be affected by changes in diagnostic techniques.

2.4.1 *Results of ecological studies*

Overall, the ecological studies do not provide indications of an increase in incidence of gliomas, meningiomas, acoustic neuromas and parotid gland tumours that might be associated with the increase in mobile telephone use that started in the mid-1990s. The effects observed, if any, are inconsistent: in some studies an increase in tumour incidence was observed in some age- or gender groups, while in others a decrease or no change at all was found. Undoubtedly there are differences in diagnostics and in the quality and completeness of the registries, especially in the earlier periods. The data from the later periods also do not show consistent changes.

2.4.2 *Conclusions on ecological studies*

The ecological studies do not provide any evidence for an association between an increase in mobile telephone use, or an increase of exposure to radiofrequency electromagnetic fields in general, and an increased risk for tumours in the brain and head and neck region.

2.5 Tumour incidence in the Netherlands

The Committee has obtained an update of the data for glioma and parotid gland tumour incidence in the Netherlands that was published in the previous report. The most recent data are now from 2012 and a breakdown is made in 10-year age groups instead of the 20-year groups in the previous report.[1] Data for other tumours are not provided, since for those the registration is not complete.

2.5.1 *Glioma*

For gliomas, the age-corrected overall incidence shows an upward trend over the period 1989-2012 (Figure 2a). The age-stratified data indicate no increasing trend in the last 15-20 year in the age groups up to 60 years (Figs 2b-2c), but in the age groups over 60 years a consistent increase in glioma incidence is present (Figure 2d). According to the investigators of the Netherlands Cancer Registry, that provided these data, the increase is mainly the result of improvements in diagnostics and in the last decade especially by the identification of glioblastomas after introduction of the Stupp treatment plan, which stimulated physicians to better select patients for treatment. This conclusion is strengthened by an initial increase in the number of unspecified central nervous system tumours that would be the result of improved diagnostics followed by a relative decrease after introduction of the Stupp treatment plan. (Ho, personal communications 11-12-2015 and 14-03-2016, and Ho et al. (2014)[48]).

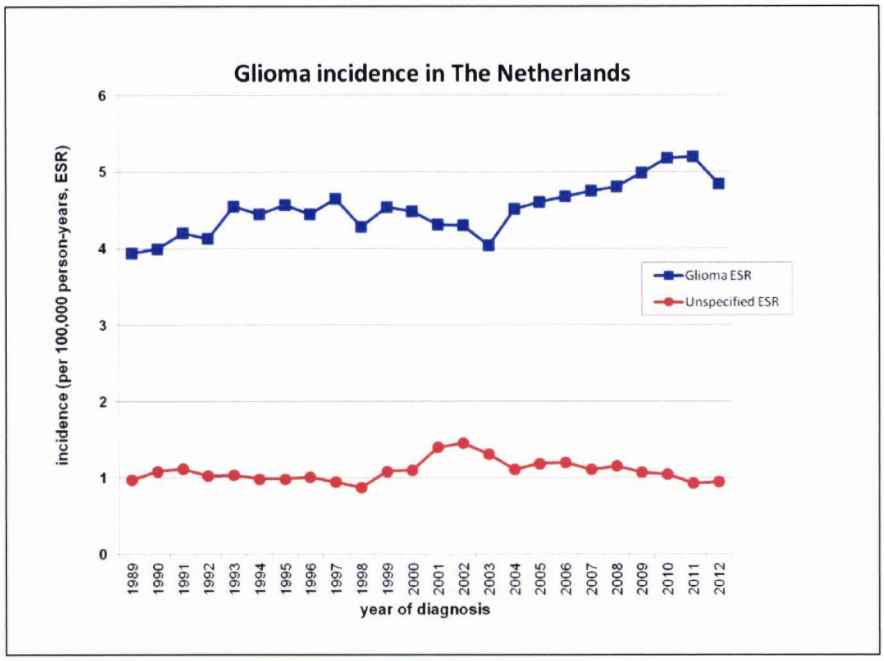

Figure 2a Incidence of gliomas and unspecified central nervous system tumours in the Netherlands from 1989-2012 for all age groups combined, age-corrected using the European Standard Population*. Source: Netherlands Cancer Registry managed by CCCNL.

* The incidence of cancer is the number of new cases registered in a certain period (often 1 year). In order to follow the incidence over time or to compare it between regions, the incidence is often presented as the crude rate, the absolute number of new cases per 100,000 persons per year. Since the crude rate will often be higher when there are relative many older people in a region (the cancer incidence is higher with older people) it is customary to standardize the incidence rate for the age distribution. This is usually done using either the European or world standard population, resulting in the 'European standardized rate'(ESR) or the 'world standardized rate'(WSR).

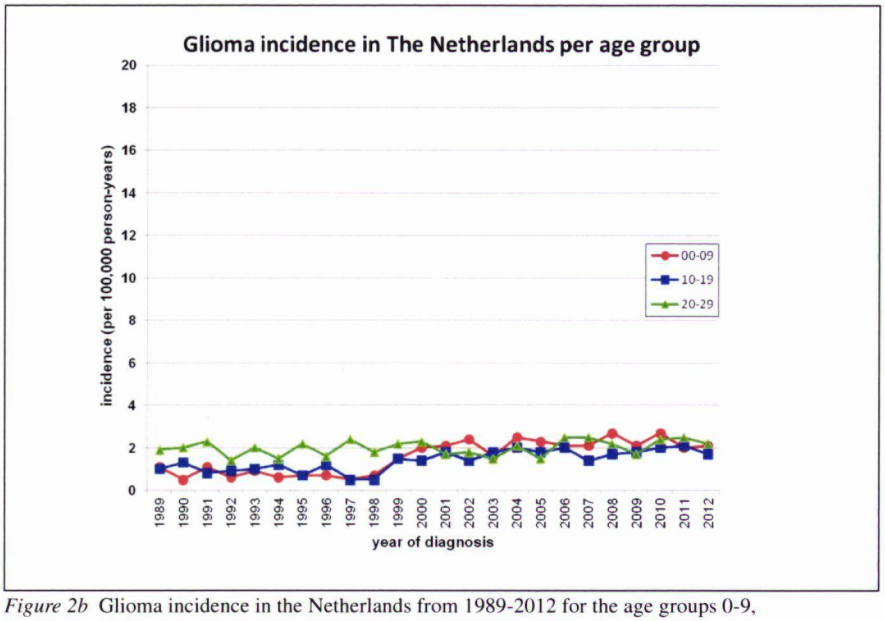

Figure 2b Glioma incidence in the Netherlands from 1989-2012 for the age groups 0-9, 10-19 and 20-29 years. Source: Netherlands Cancer Registry managed by CCCNL.

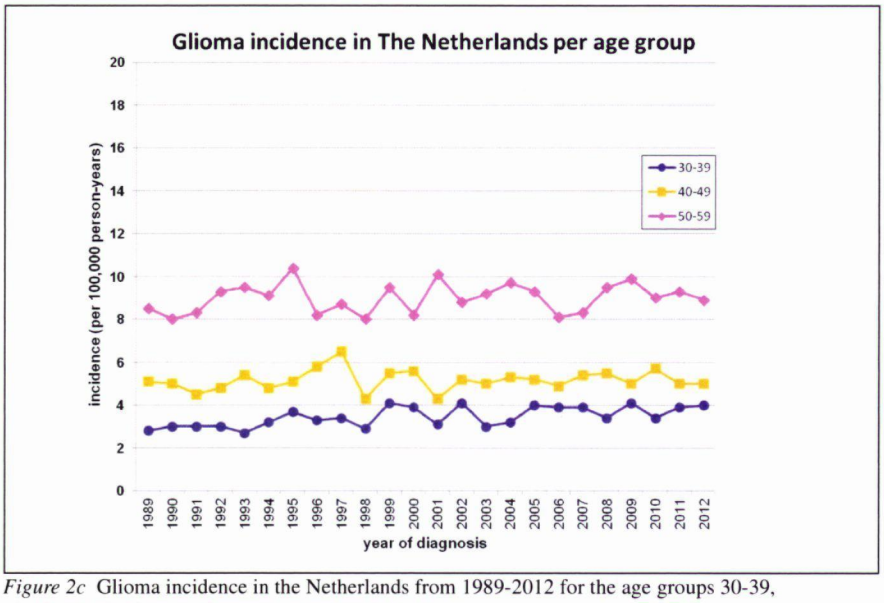

Figure 2c Glioma incidence in the Netherlands from 1989-2012 for the age groups 30-39, 40-49 and 50-59 years. Source: Netherlands Cancer Registry managed by CCCNL.

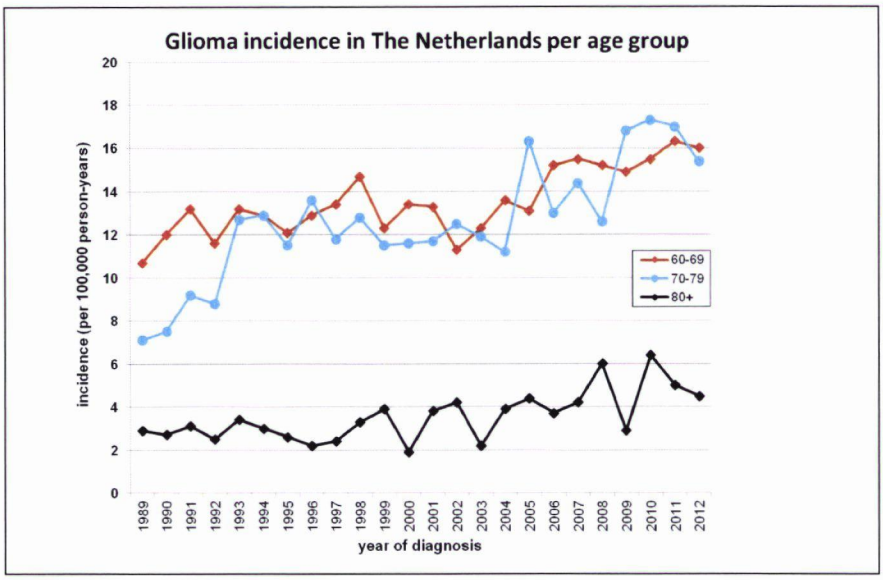

Figure 2d Glioma incidence in the Netherlands from 1989-2012 for the age groups 60-69, 70-80 and 80+ years. Source: Netherlands Cancer Registry managed by CCCNL.

2.5.2 *Parotid gland tumours*

The incidence of parotid gland tumours in the Netherlands shows a slight upward trend over the entire period 1989-2012 overall (Figure 3a).

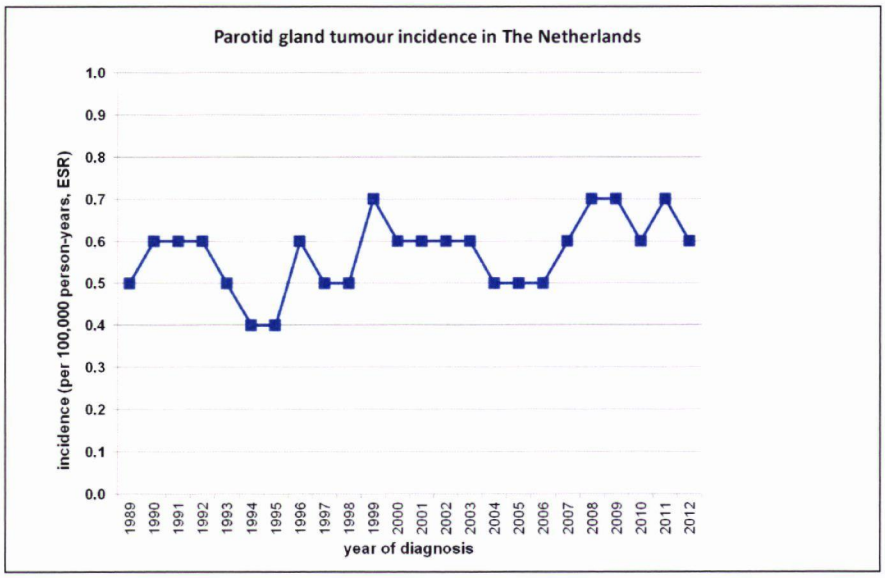

Figure 3a Incidence of parotid gland tumours in the Netherlands from 1989-2012 for all age groups combined, per 100,000 person-years, age-corrected using the European standardized rate. Source: Netherlands Cancer Registry managed by CCCNL.

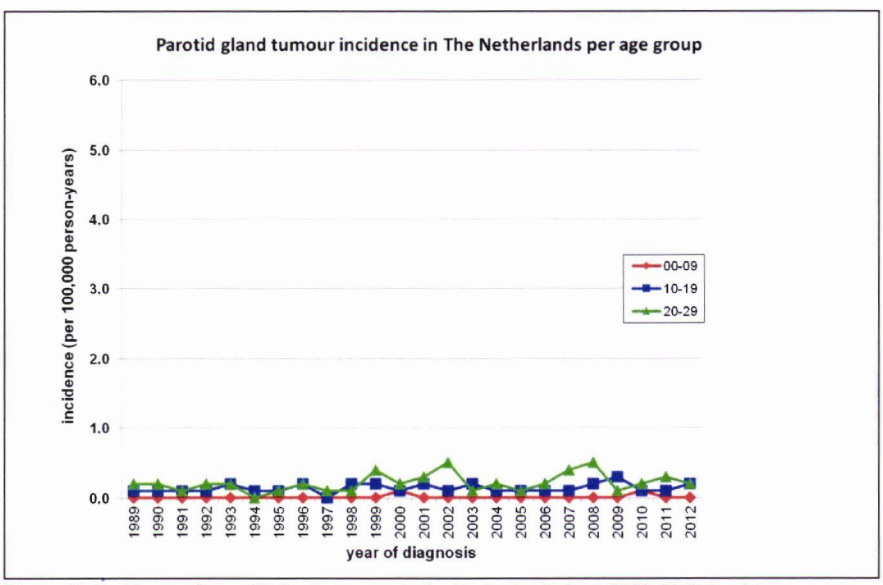

Figure 3b Incidence of parotid gland tumours in the Netherlands from 1989-2012 for the age groups 0-9, 10-19 and 20-29 years. Source: Netherlands Cancer Registry managed by CCCNL.

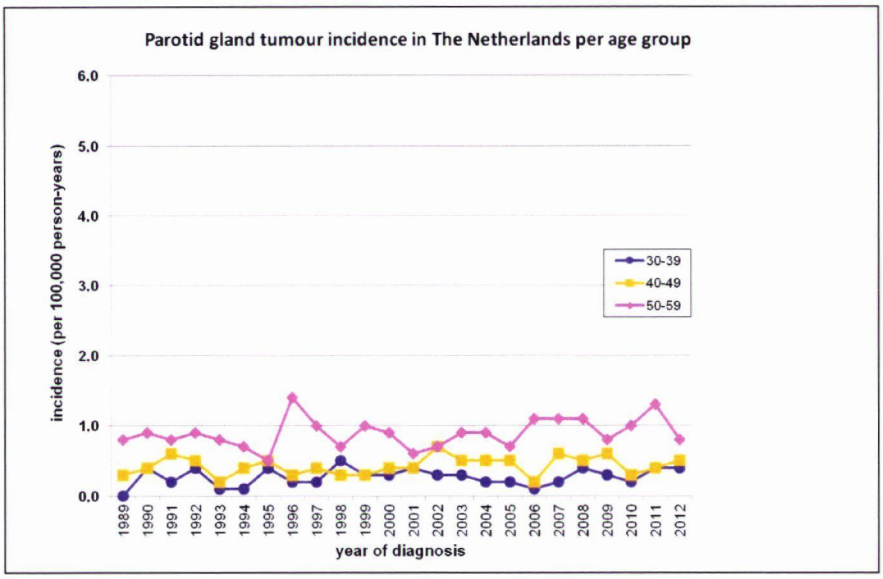

Figure 3c Incidence of parotid gland tumours in the Netherlands from 1989-2012 for the age groups 30-39, 40-49 and 50-59 years. Source: Netherlands Cancer Registry managed by CCCNL.

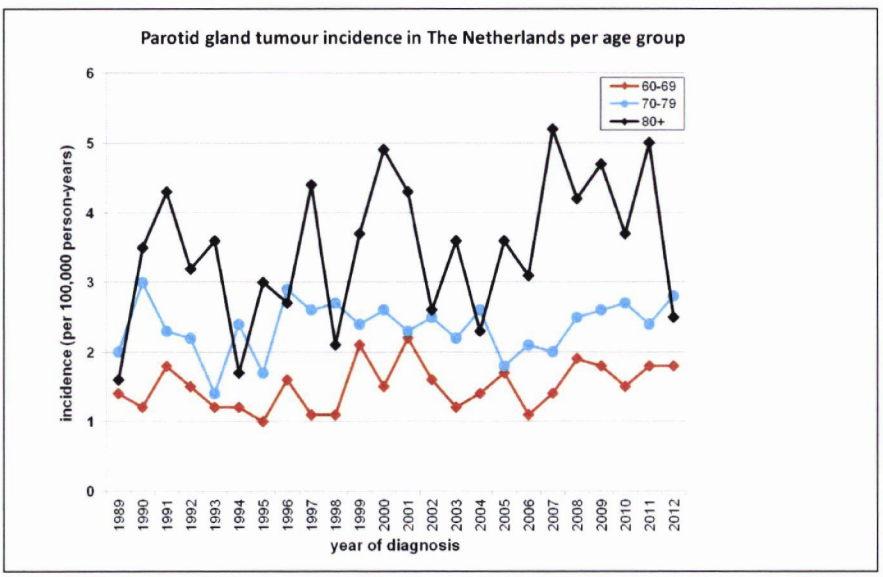

Figure 3d Incidence of parotid gland tumours in the Netherlands from 1989-2012 for the age groups 60-69, 70-79 and 80+ years. Source: Netherlands Cancer Registry managed by CCCNL.

2.5.3 Conclusions

The overall age-standardized glioma incidence in the Netherlands shows an upward trend that started already before the 1990's, when mobile phones were only available to very few people. This trend is mainly driven by the older age groups (60+). There are no indications that the massive use of mobile telephones that started in the mid 1990's and increased to use in 100% of the population in the mid 2000's (Figure 1) has led to an acceleration of the increase in glioma incidence. Assuming that the 'early adopters' of mobile phones were in the age categories of 20-30 and 30-40 years some 15 years ago, and there would be a latency time of about 5 years (which, according to current knowledge, is not very likely, it presumably is much longer), then an acceleration of the increase in tumour incidence might crudely be expected in the age categories of 30-40 and 40-50 years. Increased incidences are not seen for these age groups, but only in the >60 years age groups. These might be explained by improved diagnostic procedures. In view of the presumed long latency times of gliomas, a longer follow-up might be necessary.

For parotid gland tumours there seems to be a slight upward trend throughout the entire period of 1989-2012, but there is considerable scatter in the data, for a large part because of the very low incidence of this type of tumour. This is even more visible in the data for the different age groups. Also for parotid gland tumours, there are no indications that the massive use of mobile telephones has led to an increase in incidence in the Netherlands.

Chapter 3

Recent experimental animal data

3.1 Systematic search

On June 30, 2015, a systematic search was performed for studies published after the publication of the report of the Committee on the systematic analysis of the experimental animal data. This search was an update of the previous search done up to September 13, 2012. The following search protocol was used:

(radiofrequency OR radio waves OR radio-waves OR cellphone* OR cell phone* OR cellular *phone* OR mobile phone* OR cellular phone[MeSH Terms] OR telephone, cellular[MeSH Terms]) AND (animal OR rat OR mouse OR rats OR mice OR murine) AND (cancer OR carcinogen* OR tumour* OR tumor* OR neoplasm* OR benign OR malignant OR malignancy) NOT ("in vitro"[Publication Type] OR hyperthermia OR ablation OR imaging) AND ("2012/09/14"[Date - Entrez] : "3000"[Date - Entrez])

This resulted in 53 hits. A first inspection on the basis of the titles resulted in 3 papers that could potentially be used. Of the excluded 50 papers, 8 were in vitro studies, 7 were on treatment, 5 were reviews and 30 were on other topics.

The three selected papers were further inspected on the basis of the abstract or full text. This resulted in one paper that was to be fully systematically evaluated in the same way as the studies in the second report of the Committee.[2] Of the

papers not included, one was on structural damage to the brain and one was on treatment.

3.2 Results of the retrieved study

The study that was found through the systematic search was a replication of a study described in the previous report.[2] In that original study, Tillman et al. (2010)[49] exposed pregnant mice to a UMTS signal starting at the 6th day of pregnancy, at a power density of 4.8 W/m^2, corresponding to a whole-body SAR of 0.4 W/kg.[50] On the 14th day of pregnancy they were injected with the carcinogen ethylnitrosourea (ENU). After birth, UMTS exposure of the offspring continued until the age of 69 weeks. The researchers observed increases in the incidence of liver and lung tumours, but suggested that at least the increased rate of liver tumours might have been influenced by an infection of *Helicobacter hepaticus*. They further considered the observations preliminary and suggested replication. The Committee commented in the report on animal carcinogenesis that it agreed with that suggestion, but also that it was difficult to interpret the findings because the proper control group, ENU treatment followed by sham exposure, was missing.

Lerchl et al. (2015)[50] performed a replication of the study of Tillman et al. (2010).[49] They used larger groups and included all proper control groups. Moreover, care was taken to use only animals in which no infection with *Helicobacter hepaticus* was present. They also added two SAR levels in order to investigate a possible exposure-response relationship, and exposed the animals to 0 (sham), 0.04, 0.4 (as in the Tillman et al. study) or 2 W/kg. They investigated the incidence of 23 tumour types and observed a significant enhancement in four of them (benign brochiolo-alveolar adenoma, malignant brochiolo-alveolar carcinoma, malignant hepatocellular carcinoma, malignant lymphoma). However, for none of these tumour types a consistent relation of incidence with exposure level was found. Surprisingly, the highest level showed the least effects. Nevertheless the study did confirm the results of Tillmann et al. (2010)[49] in that it showed an effect of RF exposure on ENU-induced tumours.

3.3 Evaluation of the retrieved study

In the previous report[2] the Committee developed a quality assessment system for animal studies that evaluates whether there are possible threats to the internal and external validity of the study. The results of the evaluation of the quality of the

Lerchl et al. (2015) study, following the same protocol as described in the previous report[2], is shown in Table 7.

Table 7 Overview of the scores for the internal and external validity of the relevant animal study.

Authors	Brief results	Internal validity		External validity	
		Influence	Comment	Influence	Comment
Multiple tumours, non-transgenic animals					
Lerchl et al. (2015) [50] Replication of Tillman et al. (2010)[49]	Increased number of lung and liver tumours, no dose-response; no effect other tumours				

The blue colour indicates that threats to the internal and external validity of the study are considered low.

3.4 Discussion and comparison with previous results

Lerchl et al. (2015)[50] conclude that RF exposure has a promoting effect on ENU-induced carcinogenesis and suggest that perhaps changes in metabolism that are induced by tissue warming resulting from the absorption of RF energy may be an explanation for the observations. They suggest that for instance the uptake of ENU by the foetuses could have been higher due to an increased metabolism. However they do not provide any data to support this hypothesis and it is inconsistent with the absence of any exposure-response effect.

In the previous report, the Committee described the results of its initial systematic review on animal carcinogenesis studies.[2] The initial systematic literature search revealed a substantial body of 54 animal studies on the carcinogenesis of exposure to RF fields. In 23 studies the effect of exposure to RF EMF alone had been investigated. A variety of animal models and tumour types had been used, as well as a number of different types of RF signals, although the focus has been on the types of signals used in modern mobile telecommunication. Exposure duration was from several weeks up to two years, and the follow-up time generally lifelong. In addition, 24 studies investigated the modulating effects of RF exposure on carcinogenesis induced by various well-known carcinogenic compounds, and another seven studies the effect of RF exposure on the growth of implanted tumours. These data cover a wide range of experimental situations and may thus provide a reasonably well insight into the effects of RF exposure on carcinogenesis in rodents.

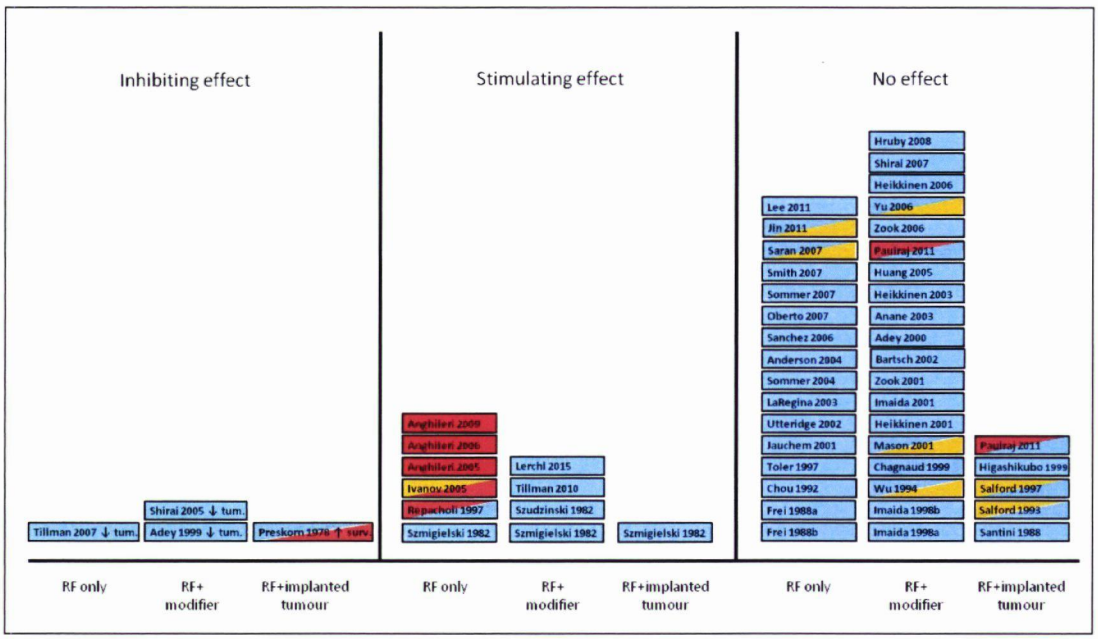

Figure 4 Overview of the animal studies included in the systematic analysis, ordered by effect outcome and type of exposure, and colour coded for internal (upper) and external validity (lower). Red: threat to validity considered high; blue: threat considered low; yellow: unknown.

The analysis of the quality of the studies, as reflected in the possibility that the internal or external validity of the studies could be affected, showed that most of the studies are of adequate design. Figure 4, updated from the previous report to include the Lerchl et al. (2015)[50] study, gives an overview of the studies included in the systematic analysis, ordered by effect outcome and type of exposure, and colour coded for internal (upper) and external validity (lower).

In eight studies various issues resulted in a negative appraisal (indicated in red in the figure) and these studies were consequently excluded from the overall analysis (one paper contained two separate studies).[51-57] Of the remaining 47 studies, six showed an increase in the incidence of several types of tumours.[49, 50, 58, 59] Four of these were closely linked and performed by the same research group of Szmigielski et al. and published in two papers.[58, 59] These authors used rather high exposure levels and could not exclude thermal effects. The fifth study is the Tillman et al. study[49] that found an increased incidence of chemically-induced lung tumours, but lacked a proper control group. The authors considered it to be a

preliminary study that needed to be replicated, which has now been done.[50] A further three studies found a decreased rate of tumour growth in RF EMF exposed animals. [60-62] There is no mechanistic explanation for this. In the majority of the studies, however, 38 in total, describing experiments on a range of tumour types and in different species, no effect on carcinogenesis has been observed.[63-100]

It may be that the observed responses in the Tillmann et al. (2010)[49] and Lerchl et al. (2015)[50] studies are typical only for the specific type of mouse used, a cross between two different mouse strains. No effect of life-long RF exposure on ENU-induced carcinogenesis was observed in a number of studies using different strains of rats[61,62,80,85,86,89] as described in the previous report of the Committee.[2] Animal models that use chemical or physical carcinogens are extremely difficult to translate to the human situation, since the studies are designed in such a way as to provide a sufficient rate of carcinogenesis to investigate modifications of the exposure conditions, i.e. the dose of the carcinogen is relatively high and/or the specific animal model used has an increased incidence of the particular type(s) of cancer compared to other models. Nevertheless, taken together, the Tillman et al. (2010)[49] and Lerchl et al. (2015)[50] studies do provide an indication for a promoting effect of RF fields. The Committee therefore feels that its conclusion from the previous report that "it is unlikely that long-term continuous or repeated exposure to RF EMF may have initiating or promoting effects on the development of cancer" should be changed to "it is unlikely that long-term continuous or repeated exposure to RF EMF may have initiating effects on the development of cancer, but a possible promoting effect warrants further investigation".

Chapter 4

Discussion and conclusions

4.1 The epidemiological evidence

The Committee concludes that the results of the epidemiological studies published since the previous report do not provide more clarity on the question of whether frequent and/or long term use of a mobile phone is associated with induction or promotion of tumours in the head and neck region.

The newer Hardell studies, which were in part pooled analyses of their previous studies, provide similar information as the previous ones: an increased risk of primarily gliomas and acoustic neuromas associated with mobile phone use. However, it has been pointed out in the previous report that the Hardell studies suffer from internal inconsistencies and this has not changed in the more recent studies. Therefore the Committee still gives the Hardell studies less weight in the overall evaluation of the epidemiological data. The recent studies from other research groups provide mixed results. A French case-control study provides weak indications for an association of mobile phone use and an increased risk of gliomas, but scores low with respect to quality. Three case-control studies found no indications for an increased risk of acoustic neuroma, but two of them score low for quality. In a study among women of an UK cohort with an adequate quality, indications for an increased risk of acoustic neuroma, but not for glioma, meningioma or pituitary tumours, were found. A new case-case study shows an

association between long-term mobile phone use and a increase in acoustic neuroma volume.

The increased risk of tumours in the head and neck region that was found in some case-control and cohort studies is not reflected by increased incidences of these tumours in ecological studies.

The data on the incidence of gliomas and parotid gland tumours in the Netherlands, which are now available up to 2012, show an increase in mainly the older population. Assuming that the 'early adopters' of mobile phones were in the age categories of 20-30 and 30-40 years some 15 years ago, and there would be an unlikely short latency time for these tumours of about 5 years, then an acceleration of the increase in tumour incidence might crudely be expected in the age categories of 30-40 and 40-50 years. An increased incidence is not seen in these age groups, but only in those of 60 years and older. This increase started already long before the massive use of mobile telephones and can be explained largely by improvements in diagnostic procedures. No acceleration of the increase has been observed after mobile phones have become in use by the majority of the population, but in view of the presumed long latency times of gliomas, a longer follow-up might be necessary.

4.2 The Bradford Hill considerations

In observational studies such as the epidemiological studies described in this and in the previous report, the quality of exposure assessment is crucial, especially in deriving exposure-response relations.[101] Moreover, the extent of selection bias and the adjustment for confounding factors are important in assessing the evidence for causality of associations. A standard tool in assessing evidence for causality are Bradford Hill's considerations.[8] Of these, in more recent epidemiological literature, strength, consistency, temporality, biological gradient (or exposure-response) and biological or physical plausibility are considered. It should be borne in mind that when these items are found to be present, this is considered to increase the likelihood of causality, but when they are not found, this does not prove that there is no causality.

Strength

A relative risk or odds ratio higher than 2 is usually considered to be a relatively strong association. Most relative risks observed in the studies discussed in this

and the previous report are lower than 2. It is likely that in the studies described, misclassification of exposure occurs. This will mostly lead to underestimation of the odds ratio, thus decreasing the strength of the observed association. Nevertheless, an odds ratio of less than 2 could also be indicative of causality if it is consistently observed. This is not really the case in the studies described.

Consistency

Consistency of results from different studies strengthens the causality argument. However, the consistency across and within the studies discussed in this and in the previous report is not very high. In several studies some increased risks have been observed in subgroups, while in others decreased risks were found. Mostly, however, no increased or decreased risks were observed. However, where one would expect the effect to occur if it exists, such as on the ipsilateral side of the exposure after longer or heavier exposure, some consistency might be perceived.

Temporality

This refers to the fact that the occurrence of the disease should always follow the exposure. In case-control studies exposure is always measured retrospectively, so temporality can never truly be addressed. Prospective cohort studies could provide more insight into this, but these are currently not available. So no conclusions on temporality can be made.

Biological gradient or exposure-response

Exposure-response relationships can only be assessed if exposure can be measured adequately and with sufficient precision.[101] However, since the case-control studies used questionnaires to retrospectively assess exposures which often occurred long ago, recall bias will decrease the accuracy of exposure assessment. Where in the INTERPHONE studies described in the previous report[1] an increased risk was observed, this was only in the highest out of 10 exposure categories for cumulative call time.[22, 32] This does not constitute a clear exposure-response relationship. No increased risks were found for cumulative number of calls. Hardell observed several exposure-response relationships in the analysis of time since first use and cumulative use for gliomas, also in the more recent studies.

Plausibility

This refers to the understanding of the biological model underlying a true association between mobile phone use and brain tumours. Many reviews have concluded that there is no known biological model to explain a relationship between mobile phone use and an increased risk of cancer.[102-105] Also the results of the animals studies described in this report do not support an effect. However, knowledge on a biological model is not a prerequisite for concluding on a causal relationship.

In conclusion, application of the Bradford Hill considerations to the available epidemiological data described in this and in the previous report is not supportive of a causal relationship between the use of mobile phones and the occurrence of tumours in the head. This may be because there really is no causal relationship, but it may also reflect inadequacies of the methods used in the studies up to date or in the ability to measure exposure and outcome.

4.3 The evidence from experimental animal studies

Concerning the experimental animal data, only one new study has been published since the previous report. It is a replication of an earlier report that suggested an increased incidence of liver tumours in a very specific mouse model of tumour development after prenatal exposure to the carcinogen ethylnitrosourea (ENU), but it was hampered by a missing control group and a bacterial infection. The replication did include all proper controls and confirmed the earlier results – an increase in the incidence of liver tumours – but also an increase in two specific types of lung tumour and in lymphomas. ENU is a carcinogen known to induce neurogenic tumours, so it is remarkable that out of the 23 types of tumours investigated, the four that showed an enhanced incidence were not of the expected type. Studies into the effect of RF + ENU on neurogenic tumours were discussed in the previous report and showed no effect of RF exposure. Also studies on the effects of long-term exposure to RF EMF alone or in combination with a number of carcinogens did not show any effect of RF EMF on the development of tumours.

The Committee wishes to stress that the effects in rodents described here have been observed in a very specific mouse model with exposure to a carcinogen. Whether this has any predictive value of effects in humans is unknown.

The Committee concludes that with the result of the replication study, its previous conclusion that "it is highly unlikely that long-term continuous or repeated exposure to RF EMF may have initiating or promoting effects on the development of cancer" will have to be changed in "there is no evidence that long-term continuous or repeated exposure to RF EMF may have initiating effects on the development of cancer, but a possible promoting effect warrants further investigation".

4.4 Overall conclusion on carcinogenicity

Overall, the data from several epidemiological studies provide some indications for an association between long-term and/or intensive use of a mobile phone and an increased incidence of tumours in the brain and head and neck region, but the evidence is weak and inconsistent. The incidence data in the Netherlands and in other countries worldwide do not provide any support for such association. It is possible that the exposure to RF EMF resulting from the use of mobile phones plays a role in an association, should it exist, but the Committee considers it unlikely that such exposure actually induces tumours. Animal data do not provide evidence for induction of tumours, only a weak indication for a possible promotion effect.

These conclusions are different from those of IARC.[5] Concerning the epidemiological data, IARC concludes: "There is limited evidence in humans for the carcinogenicity of radiofrequency radiation. Positive associations have been observed between exposure to radiofrequency radiation from wireless phones and glioma, and acoustic neuroma." [4] According to IARC's definition of "limited evidence", this means that "a positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence." The conclusion of IARC with respect to the animal data is: "There is limited evidence in experimental animals for the carcinogenicity of radio frequency radiation." Taking into account the epidemiological and experimental data, the Committee considers a causal interpretation unlikely and feels that the combination of bias, confounding and chance might be an explanation for the observations.

4.5 Ongoing and future studies

So far most studies have only been able to evaluate the effects of relatively short duration of exposure to RF EMF and were limited informative at best for insight in the development of relevant tumours with long latency times. Some epidemiological studies have follow-up times of more than 13 years, but with very few subjects in the highest exposure categories. The Committee therefore considers it very important that ongoing cohort studies evaluating the health effects of mobile phone use be continued in order to provide more conclusive human evidence. The exposure characterization in all currently available studies is very poor. It is therefore important that ongoing and future studies incorporate more accurate and objective assessment of RF exposure. This is even more important since personal exposure to RF EMF continues to change due to evolving ways of use and new mobile telecommunication devices.

4.6 Reduction of exposure

The available data do not allow drawing conclusions on whether there is an association between an increased carcinogenic risk and any form of accumulation of exposure, for instance expressed in the total call time, or the total amount of energy deposited by the electromagnetic fields generated by the phone in the head or in any other body part. So it is not possible to state whether a higher or longer exposure is less safe than a lower or shorter exposure. The Committee therefore considers the value of any measures to reduce exposure unclear. However, it is possible that some individuals would like to reduce their exposure, despite the conclusion of the Committee that there is no consistent evidence for an increased risk for tumours in the brain and other regions in the head associated with mobile phone use. The Knowledge Platform Electromagnetic Fields provides a number of suggestions for exposure reduction.[106]

Despite the fact that no exposure-response relationships have been observed, the Committee would like to repeat the suggestion from the previous report[1] to apply the ALARA principle to exposure to RF EMF, meaning that exposures should be As Low As Reasonably Achievable. There is no need for any device to transmit with greater power or for a longer period of time than needed for an adequate connection. This is fully in line with the suggestions from the Health Council's advisory report *Prudent precaution*.[3]

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Annexes

Annex **A**

The Committee

The membership of the Electromagnetic Fields Committee at the time of preparation of this advisory report was as follows:

- Prof. G.C. van Rhoon, *chair*
  Professor of Physical Aspects of Electromagnetic Fields and Health, Erasmus University Medical Centre Rotterdam
- Prof. A. Aleman
  Professor of Cognitive Neuropsychiatry, University of Groningen
- Dr. S. Le Cessie
  Statistician, Department of Clinical Epidemiology and Department of Medical Statistics, Leiden University Medical Center (*since 01-12-2015*)
- Prof. J.J.G. Geurts
  Professor of Translational Neuroscience Research, VU University Medical Centre, Amsterdam (*since 01-01-2016*)
- Dr. A. Huss
  Institute for Risk Assessment Sciences, University of Utrecht (*since 01-01-2016*)
- Prof. H. Kromhout
  Professor of Epidemiology of Health Effects from Exposure to Electromagnetic Fields, Institute for Risk Assessment Sciences, University of Utrecht
- Prof. F.E. van Leeuwen
  Professor of Cancer Epidemiology, Free University of Amsterdam; Head,

Division of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam (*until 31-12-2015*)

- Prof. H.F.J. Savelkoul
  Professor of Cell Biology and Immunology, Wageningen University
- Dr. R. van Strien
  Epidemiologist, Municipal Health Services, Amsterdam (*since 01-01-2016*)
- Prof. W.J. Wadman
  Professor of Neurobiology, University of Amsterdam
- D.H.J. van de Weerdt, physician
  Toxicologist and specialist in environmental medicine, Central Gelderland Municipal Health Services (GGD), Arnhem (*until 31-12-2015*)
- Prof. A.P.M. Zwamborn
  Professor of Electromagnetic Fields and Health, Eindhoven University of Technology; Physicist, TNO (Netherlands Organisation for Applied Scientific Research), The Hague (*until 31-12-2015*)
- Dr. G. Kelfkens, *structurally consulted expert*
  Physicist, National Institute for Public Health and the Environment, Bilthoven
- Prof. E. Lebret, *observer*
  Professor of Environmental Health Impact Assessment, Institute for Risk Assessment Sciences, Utrecht University; Knowledge Platform Electromagnetic Fields, Bilthoven (*until 31-12-2015*)
- Dr. M.J.M. Pruppers, *observer*
  Physicist, Knowledge Platform Electromagnetic Fields, Bilthoven
- J. Robijns, *observer*
  Ministry of Economic Affairs, The Hague
- R.P.R. Schutte, *observer*
  Ministry of Infrastructure and the Environment, The Hague
- Dr. H.F.G. van Dijk, *scientific secretary*
  Biologist, Health Council of the Netherlands, The Hague (*since 01-09-2015*)
- Dr. E. van Rongen, *scientific secretary*
  Radiobiologist, Health Council of the Netherlands, The Hague

Prof. I.A. Kreis, epidemiologist, and Palles health research and consultancy assisted in the extraction and scoring of the data. The registration teams of the Comprehensive Cancer Centre Netherlands and Comprehensive Cancer Centre South collected the data for the Netherlands Cancer Registry and the scientific staff of the Comprehensive Cancer Centre Netherlands provided the analysis of the data.

The Health Council and interests

Members of Health Council Committees are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the chairperson and members of a Committee and for the President of the Health Council. On being invited to join a Committee, persons are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee's work. It is the responsibility of the Health Council to assess whether or not someone can become a member. An expert who has no financial but another clearly definable interest, can become a member under the restriction that he will not be involved in the debate on the subject to which his interest relates. If a person's interest is not clearly definable, he can sometimes be consulted as an expert. Experts working for a ministry or governmental organisation can be structurally consulted. During the inaugural meeting the declarations issued are discussed, so that all members of the Committee are aware of each other's possible interests.

Annex **B**

Evaluation of the quality of the studies

Table B1 shows the method used to evaluate cohort, case-control and case-case studies. Ecological studies were not evaluated.

Questions 1-4 are contributing to the domain of selection, with a maximum score of 34; question 5 contributes to the domain of diagnosis, with a maximum score of 4; questions 6-14 contribute to the domain of exposure, with a maximum score of 69; questions 15 and 16 contribute to the domain of confounding, with a maximum score of 16; and question 17 contributes to the domain of conflict of interest, with a maximum score of 5.

Table B1 Evaluation system used for cohort, case-control or case-case studies on mobile phone use and head and neck tumours.

No.	Question	Evaluation		Score	Remarks
	Selection				
1	Did cases & controls come from the same source population?	a	No or unknown	0	Consider Berkson's bias if hospital based.
		b	Yes	12	
		c	Not applicable (cohort or case-case)	12	
2	Were the same inclusion/exclusion criteria applied to cases and controls?	a	No or unknown	0	
		b	Yes	6	
		c	Not applicable (cohort or case-case)	6	
3	What was the % response of the cases?	a	< 76% or unknown or unclassifiable	0	Include deceased cases and refusals by physician in (re)calculated response rates
		b	76-90%	4	
		c	> 90%	8	
		d	Not applicable (cohort or case-case)	8	
4	Was the absolute difference in % response between cases and controls <20%?	a	No or unknown	0	
		b	Yes	4	
		c	Not applicable (cohort or case-case)	8	
	Diagnosis				
5	Was the cancer diagnosis valid?	a	No or unknown	0	If they use cancer registry they probably have historogy and imaging but if they have glioma vs maningioma they certainly have histology
		b	Yes, but imaging only	1	
		c	Yes, but imaging plus location only	2	
		d	Yes, including histology	3	
		e	Yes, including histology and location	4	
	Exposure				
6	Could the type of administration of the (exposure) questionnaire lead to observer bias?	a	Participant or proxy, interview (in person or by phone) administered	0	
		b	Participant or proxy, self administered	5	
		c	Register-based	5	
7	Were all cases and controls treated equally?	a	No or not provided	0	No is if there is clearly a different data collection protocol or people involved between the groups
		b	Yes	5	
		c	Yes as is cohort study	5	
8	Was there potential for non-differential misclassification?	a	Yes: register based data-collection	0	
		b	somewhat: self administered data collection	5	
		c	No: interview-based data collection	5	

9	Completeness of type mobile telephone history?	a	Total of 2 points	2	Accumulate points for phone type history Mobile phone, non-specified analogue or digital: 3 points Mobile phone, specified analogue or digital: 4 points Cordless or DECT phone: 2 points Change in phone type: 3 points
		b	Total of 3 points	3	
		c	Total of 4 points	4	
		d	Total of 5 points	5	
		e	Total of 6 points	6	
		f	Total of 7 points	7	
		g	Total of 8 points	8	
		h	Total of 9 points	9	
10	Did the measure of exposure include frequency and duration and start date?	a	No	0	
		b	Start date or call-duration or frequency	4	
		c	Start date and call-duration or frequency	6	
		d	All three, but no changes	8	
		e	All three, including changes in use for all types	10	
11	Did the exposure assessment include lateralisation of phone use?	a	No	0	
		b	Indirectly via handedness	5	
		c	Yes, directly via questions and allowing for combinations	10	
12	Were changes over time considered in the analysis?	a	No	0	If changes asked for and total hours called calculated: assumed changes incorporated
		b	Yes	5	
13	Was the exposure questionnaire validated or was reliability tested?	a	No or unknown	0	
		b	Validated in another (related) study such as subsample	5	
		c	Provider data verified	10	
14	Was the exposure assessed before the cancer diagnosis (thus avoiding recall bias)?	a	No (case-control)	0	
		b	Yes (cohort or nested case-control)	10	
	Confounding				
15	Were confounders adjusted in a correct way?	A	No or unknown	0	Potential confounders: age, sex
		b	Yes	8	
16	Could residual confounding influence the results?	A	Yes or unknown	0	As little known about potential confounders, this is likely to always be partly true
		b	Partly	4	
		c	No	8	
	Conflict of interest				
17	Was there evidence of potentail conflict of interest?	A	Yes	0	
		b	Yes, but with firewall	3	
		c	No	5	

The results of the scores per question are presented in Tables B2, B3 and B4. These are the combined scores for the two evaluators. These final scores were the result of independent scoring, comparison and mediation.

Table B2 Results of the quality scores for the cohort study.

	Question																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Benson et al. (2013)[12]	c	c	d	c	e	b	c	b	b	c	a	a	a	b	b	b	c

Table B3 Results of the quality scores for the case-control studies.

	Question																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Hardell et al. (2013)[17]	b	b	b	b	e	a	b	c	h	e	c	b	a	a	b	b	c
Hardell & Carlberg (2015)[18]	b	b	b	b	e	a	b	c	h	e	c	b	a	a	b	b	c
Carlberg et al. (2013)[20]	b	b	b	b	e	a	b	c	h	e	c	b	a	a	b	b	c
Coureau et al. (2014)[30]	b	b	a	a	d	a	a	c	f	e	c	b	a	a	b	b	c
Feltbower et al. (2014)[31]	a	a	a	b	d	a	b	c	b	b	a	a	a	a	a	a	c
Hardell et al. (2013)[19]	b	b	c	b	e	a	b	c	h	e	c	b	a	a	b	b	c
Corona et al. (2012)[34]	a	a	b	b	c	a	b	c	f	d	c	b	a	a	a	a	c
Moon et al. (2014)[35]	a	a	b	a	e	a	b	c	f	e	c	b	a	a	a	a	c
Pettersson et al. (2014)[36]	b	b	b	b	c	b	b	b	h	e	c	b	a	a	b	b	c

Table B4 Results of the quality scores for the case-case study.

	Question																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Moon et al. (2014)[35]	c	c	d	c	e	a	b	c	f	e	c	b	a	a	a	a	c

These scores lead to the overall scores for the domains of selection, diagnosis, exposure and confounding which are presented in Table B5 as percentage of the maximum score for each domain.

The Committee weighted the domains for the overall rating as 4 (Selection) : 1 (Diagnosis) : 4 (Exposure) : 1 (Confounding) : 0 (Conflict of interest). The Committee considered Conflict of Interest to be important, but it could be poorly assessed due to missing information. The information that was used for scoring were the financial interests declared in the publications. In some cases, earlier publications about the same study revealed interests that were not declared later.

This may be correct, as at the time of the later publication the funding may have ceased, but some level of conflict of interest could still be suspected. The Committee felt that the impact of such financial ties can be widely different and there was insufficient information to take this into account. Also, non-financial interests and professional commitment to an opinion about an association between mobile phone use and brain cancer could also influence the presentation of the results. Again this could not be measured. Therefore the score for Conflict of Interest was not taken into account in the overall score but is only given for information.

The final overall rating is given in the last column of Table B5 as a number between 0 and 10 (i.e. the total of the weighted percentage scores devided by 100). To facilitate distinguishing higher from lower rated studies, they are colour coded, but without any particular meaning of the cut-off values. Ratings of 7.0 and higher are marked green, ratings of between 3.0 and 7.0 are marked yellow, and ratings lower than 3.0 are marked red.

Table B5 Results for the evaluation of selected cohort, case-control and case-case studies.

		Domains:	Selection bias	Misclassification of outcome	Misclas-sification of exposure	Confounding	Conflict of interest	Overall score (0-10)
Reference	**Design**	**Tumour**	% of maximum obtainable score					
Benson et al. (2013)[12]	Cohort	Brain tumours combined, glioma, meningioma	100.0	100.0	50.0	75.0	100.0	7.8
Hardell et al. (2013)[17]	Ca-co	Malignant brain tumours	76.5	100.0	64.7	75.0	100.0	7.4
Hardell & Carlberg (2015)[18]	Ca-co	Glioma	76.5	100.0	64.7	75.0	100.0	7.4
Carlberg et al. (2013)[20]	Ca-co	Meningioma	76.5	100.0	64.7	75.0	100.0	7.4
Coureau et al. (2014)[30]	Ca-co	Glioma, meningioma	52.9	75.0	54.4	75.0	100.0	5.8
Feltbower et al. (2014)[31]	Ca-co	Brain tumours	11.8	75.0	25.0	0.0	100.0	2.2
Hardell et al. (2013)[19]	Ca-co	Acoustic neuroma	88.2	100.0	64.7	75.0	100.0	7.9
Corona et al. (2012)[34]	Ca-co	Acoustic neuroma	23.5	50.0	58.8	0.0	100.0	3.8
Moon et al. (2014)[35]	Ca-co	Acoustic neuroma	11.8	100.0	61.8	0.0	100.0	3.9
Moon et al. (2014)[35]	Ca-ca	Acoustic neuroma	100.0	100.0	61.8	0.0	100.0	7.5
Pettersson et al. (2014)[36]	Ca-co	Acoustic neuroma	76.5	50.0	72.1	75.0	100.0	7.2

Ca-co: case-control, Ca-ca: case-case.

Selection bias

Selection biases are distortions that result from procedures used to select subjects and from factors that influence study participation. The common element of such biases is that the relation between exposure and disease is different for those who participate and for all those who should have been theoretically eligible for the study, including those who did not participate.[107]

Maximum scores in the selection bias domain are inherently generated for the cohort and case-case studies.

In the previous report, the Committee mentioned that a striking feature of the case-control studies in this domain is the generally high response rates of the Hardell studies. In several of the studies from other groups discussed in the current report, similar high response rates have been obtained. This means that the Committee does not consider the response rates in the Hardell studies reported here as unrealistically high.

Misclassification of outcome

As in the previous report, no problems were seen for any of the studies in the domain of misclassification of outcome.

Misclassification of exposure

In the domain of misclassification of exposure the items of interest are the bias resulting from the method of collecting the information on mobile phone use and the validity of the reported information.

In the previous report it was described that in the Hardell studies exposure information was obtained by a written questionnaire followed in all cases by a follow-up interview by telephone. In some of the Hardell studies described in this report, it was stated that follow-up by telephone was done in less than 100% of cases. Telephone interviews may lead to observer bias and, hence, to differential misclassification with potential overestimation of the risks. Overall, as was also concluded in the previous report, the quality of the exposure assessment in the Hardell studies is difficult to judge.

The quality of the exposure assessment in the other studies reported here is not very high. This means that in all studies misclassification of exposure might have occurred.

Confounding

A risk factor for brain tumours is a confounder when the exposure to that factor is associated with the exposure of interest, in this case exposure resulting from the use of mobile or cordless phones.

Annex **C**

Overview of ecological studies on brain tumours

Table C1 Ecological studies.

Reference	Country	Data source	Tumour	Age	Time period	Incidence or annual percentage of change (95% CI); statistically significant in bold	Comment
Glioma's and brain tumours - post 2005							
Sehmer et al. (2014)[108]	England	National Cancer Data Repository	Glioma	>15 year	2006-2010	6.93 / 100000 (6.82, 7.04); no trend	
Kim et al. (2015)[109]	New Zealand	New Zealand Cancer Registry	Brain cancers	5-year-age subgroups; 0-9, 10-69, 70+ year	1995-2010	Glioma Men, 10-69: 0.59% (-1.84, 0.68) Women, 10-69: 0.29% (-0.88, 1.48) **Men, 10-29: -5.46 (-8.09, -2.75)** Women, 10-29: 2.69% (-6.21, 0.96) Men, 30-49: 0.16% (-2.13, 2.51) **Women, 30-49: 3.12% (1.38, 4.89)** Men, 50-69: 0.21% (-1.33, 1.78) Women, 50-69: 0.31% (-2.1, 1.52) **Men, 70+: 2.98% (0.31, 5.72)** Women, 70+: 1.76% (-0.04, 3.59)	
Aydin et al. (2012)[110]	Denmark, Norway, Finland, Iceland, Sweden	NORDCAN	Brain & CNS tumours	5-19 year	1990-2009	No trend.	

Barchana et al. (2012)[111]	Israel	National Cancer Registry	High-grade glioma		1980-1984 1985-1989 1990-1994 1995-1999 2000-2004 2004-2009	Men:	2.58 / 100,000 3.91 / 100,000 4.08 / 100,000 5.56 / 100,000 6.21 / 100,000 5.64 / 100,000	World Standard Population standardized
					1980-1984 1985-1989 1990-1994 1995-1999 2000-2004 2004-2009	Women:	1.77 / 100,000 2.49 / 100,000 3.29 / 100,000 3.46 / 100,000 3.81 / 100,000 4.06 / 100,000	
			Low-grade glioma		1980-1984 1985-1989 1990-1994 1995-1999 2000-2004 2004-2009	Men:	2.57 / 100,000 2.34 / 100,000 2.79 / 100,000 1.71 / 100,000 1.82 / 100,000 1.57 / 100,000	
					1980-1985 1985-1989 1990-1994 1995-1999 2000-2004 2004-2009	Women:	1.93 / 100,000 1.72 / 100,000 1.78 / 100,000 1.38 / 100,000 1.17 / 100,000 1.04 / 100,000	
Deltour et al. (2012)[112]	Denmark, Finland, Norway and Sweden	National cancer registries	Glioma	20-39, 40-59, 60-79 year	1979-2008	Slight increase in 60-79 year group over entire period (men and women).		
De Vocht et al. (2011)[113]	England	UK Office of National Statistics	Brain cancer	10-year age groups	1998-2007	No change in any age group.		
Hardell et al. (2010)[114]	Denmark, Norway, Finland, Iceland, Sweden	NORDCAN	Nervous system tumours		1960-2007	Men: Women:	1.02% (0.90, 1.14) 1.66% (1.56, 1.76)	
Ding and Wang (2011)[115]	Shanghai, China	Shanghai Municipal Center for Disease Control and Prevention, Shanghai Cancer Institute, Cancer Incidence in Five Continents	Brain, nervous tumours		1983-2007	Men: Women:	1.2% (0.4, 1.9) 2.8% (2.1, 3.4)	

Zada et al. (2012)[116]	USA	Los Angeles County Cancer Surveillance Program (LAC), California Cancer Registry (CCR), SEER	Glioblastoma multiforme		1992-2006	**Frontal lobe:** **Temporal lobe:** **Overlapping regions:** Parietal, occipital lobes: **Cerebellum:** **All glioma, all sites:**	**2.4-3.0%** **1.3-2.3%** **-2.0% to -2.8%** No change. **11.9%** **-0.5% to -0.8%**
Glioma's and brain tumours - pre 2005							
Doré et al. (2010)[117]	France		Central nervous system tumours		1980-2005 2000-2005	Men: Women: Men: Women:	0.2% 1.1% 0.1% 0.6%
Lönn et al. (2004)[118]	Denmark, Norway, Finland, Sweden	National cancer registries	Glioma	20-79 year	1969-1998	Men: Women:	0.7% (0.5, 0.9) 0.6% (0.4, 0.8)
Nomura et al. (2012)[119]	Osaka, Japan	Osaka Cancer Registry	Primary intracranial tumours	0->74 year	1975-2004	0-19 year: 20-74 year: >74 year:	Decrease Decrease Increase
					1995-2004	All ages:	-1.8% (-2.6, -0.9)
			Glioblastoma		1995-2004	All ages:	-1.3% (-2.8, 0.2)
			Meningioma		1995-2004	All ages:	-2.9% (-5.1, -0.5)
Deltour et al. (2009)[120]	Denmark, Finland, Norway and Sweden	National cancer registries	Glioma		1974-2003	Men: Women:	0.5% (0.2, 0.8) 0.2% (0.1, 0.5)
Muscat et al. (2006)[121]	USA	SEER	Neuronal cancer (gangliomas and similar tumour types)	≥20 year	1973-1985 1986-2002	0.01 / 100,000 (0.00, 0.02) 0.01 / 100,000 (0.01, 0.01)	
Deorah et al. (2006)[122]	USA	SEER	Brain cancer	All ages	1973-1987 1988-2001	All ages:	1.68% (91.22, 2.130) -0.44% (-0.84, -0.030)
					1973-1989 1990-2001	< 20 year:	1.91% (0.72, 3.12) 0.22% (-1.25, 1.73)
					1973-1987 1988-2001	20-65 year:	0.62% (0.00, 1.24) -0.98% (-1.57, -0.38)
					1973-1987 1988-2001	>65 year:	3.87% (2.58, 5.19) 0.08% (-0.50, 0.68)
			Glioblastoma		1973-1979 1980-1991 1992-2001	All ages:	-5.58% (-2.12, -8.91) 2.88% (1.47, 4.30) 0.321% (-1.0, 1.66)
Crocetti et al. (2012)[123]	Europe	RARECARE	Glioma	All ages	1995-2002	All ages: 0-19 year: 20-39 year: 40-59 year: 60+ year:	Stable Stable Stable Stable Increase 1995-1997, stable thereafter

Röösli et al. (2007)[124]	Switzerland	Swiss Federal Statistical Office	Brain cancer mortality	All ages	1969-2002	Men: Women:	3.7-6.7 / 100,000 2.5-4.4 / 100,000	
Menigioma's - pre 2005								
Deltour et al. (2009)[120]	Denmark, Norway, Finland, Sweden	National cancer registries	Meningioma	20-79 year	1974-2003	Men: Women:	0.8% (0.4, 1.3) 3.8% (3.2, 4.4) (after early 1990s)	
Cook et al. (2003)[125]	New Zealand	New Zealand Cancer Registry	Brain cancer, meningioma, salivary gland tumours	20-69 year	1986-1998	No increase		
Acoustic neuroma's - post 2005								
Larjavaara et al. (2011)[126]	Denmark, Norway, Finland, Sweden	National cancer registries	Acoustic neuroma	All ages	1988-2006	3.0% (2.1, 3.9) Roughly similar for age groups (0-44, 45-54, 55-64, >64 year)		Incidence stable after late 1990s, some decline after 2000
Acoustic neuroma's - pre 2005								
Nelson et al. (2006)[127]	England, Wales	National Cancer Registry	Acoustic neuroma and other benign cranial nerve tumours	All ages	1980-1983 1990-1997 1997-2000	Slight increase Steep increase Decrease		
Other tumours - post 2005								
Shu et al. (2012)[128]	Denmark, Norway, Finland, Iceland, Sweden	Swedish Cancer Registry, NORDCAN	Parotid gland tumours	>20 years	1970 2009	Sweden, men:	0.9 / 100,000 0.8 / 100,000	
					1970 2009	Sweden, women:	0.7 / 100,000 0.7 / 100,000	
					1970-2009	Nordic, men:	0.1% (-0.4, -0.2)	
					1970-2009	Nordic, women:	0.2% (-0.5, -0.1)	
Ellington et al. (2012)[129]	USA	SEER	Adenoid cystic carcinoma	All ages	1973-2007	Continuous decrease (men & women).		
Derbi et al. (2014)[130]	Western Australia	Western Australia Cancer Registry	Parotid gland cancer	All ages	1982 2009	Men:	1.8 / 100,000 2.2 / 100,000	
					1982 2009	Women:	3.1 / 100,000 3.5 / 100,000	

Annex **D**

Results from the selected publications

This Annex presents all the detailed results in tables, organized by tumour type. Statistically significant increased risks are in **boldface type**.

Glioma

Table D1 Glioma and time since first use.

Reference	Type of phone	Exposure Time since 1st use (years)			
Cohort study			Ca	RR	95%CI
Benson et al. (2013)[12]	All mobile phone	≥10	40 (571 total)	0.78	0.55-1.10
Case-control studies			Ca / Co	OR	95%CI
Hardell et al. (2013)[17]	Analogue	>1			
		>1-5	0 / 0	--	
		>5-10	2 / 10	0.6	0.1-3.1
		>10-15	25 / 51	1.4	0.7-3.0
		>15-20	39 / 86	1.4	0.7-2.7
		>20-25	48 / 80	2.1	1.1-4.0
		> 25	30 / 33	3.3	1.6-6.9
	GSM	>1	546 / 1208	1.6	0.996-2.7
		>1-5	42 / 109	**1.8**	**1.01-3.4**
		>5-10	213 / 477	1.6	0.97-2.7
		>10-15	187 / 453	1.3	0.8-2.2
		>15-20	104 / 169	**2.1**	**1.2-3.6**
		>20-25	0 / 0	--	
		> 25	0 / 0	--	

UMTS	>1	67 / 140	1.2	0.6-2.4
	>1-5	55 / 126	1.2	0.6-2.4
	>5-10	12 / 14	1.6	0.5-4.9
	>10-15	0 / 0	--	
	>15-20	0 / 0	--	
	>20-25	0 / 0	--	
	> 25	0 / 0	--	
Mobile phone	>1	548 / 1217	1.6	0.99-2.7
	>1-5	41 / 108	**1.8**	**1.002-3.4**
	>5-10	190 / 423	1.7	0.98-2.8
	>10-15	163 / 399	1.3	0.8-2.2
	>15-20	76 / 174	1.5	0.8-2.6
	>20-25	48 / 80	**1.9**	**1.1-3.5**
	> 25	30 / 33	**2.9**	**1.4-5.8**
Cordless	>1	461 / 1015	**1.7**	**1.1-2.9**
	>1-5	102 / 209	**2.0**	**1.1-3.4**
	>5-10	188 / 436	1.6	0.95-2.7
	>10-15	108 / 248	1.6	0.9-2.8
	>15-20	57 / 109	**2.1**	**1.2-3.8**
	>20-25	6 / 13	1.5	0.5-4.6
	> 25	0 / 0	--	
Digital	>1	571 / 1261	**1.7**	**1.04-2.8**
	>1-5	33 / 63	**2.6**	**1.4-4.9**
	>5-10	177 / 421	1.6	0.9-2.7
	>10-15	212 / 523	1.4	0.8-2.3
	>15-20	143 / 241	**2.2**	**1.3-3.6**
	>20-25	6 / 13	1.5	0.5-4.6
	> 25	0 / 0	--	
All wireless	>1	571 / 1261	**1.7**	**1.04-2.8**
	>1-5	32 – 61	**2.6**	**1.4-5.0**
	>5-10	163 / 378	1.6	0.98-2.8
	>10-15	184 / 466	1.3	0.8-2.2
	>15-20	110 / 231	**1.7**	**1.02-3.0**
	>20-25	52 / 92	**1.9**	**1.04-3.4**
	> 25	30 / 33	**3.0**	**1.5-6.0**
Analogue only	>1	0 / 0	--	
	>1-5	0 / 0	--	
	>5-10	0 / 0	--	
	>10-15	0 / 0	--	
	>15-20	0 / 0	--	
	>20-25	0 / 0	--	
	> 25	0 / 0	--	

	GSM only	>1	78 / 176	1.6	0.9-2.9
		>1-5	9 / 13	**3.4**	**1.2-9.5**
		>5-10	33 / 79	1.6	0.8-3.2
		>10-15	28 / 68	1.3	0.6-2.6
		>15-20	8 / 16	1.8	0.6-4.9
		>20-25	0 / 0	--	
		> 25	0 / 0	--	
	UMTS only	>1	1 / 0	--	
		>1-5	1 / 0	--	
		>5-10	0 / 0	--	
		>10-15	0 / 0	--	
		>15-20	0 / 0	--	
		>20-25	0 / 0	--	
		> 25	0 / 0	--	
	Cordless only	>1	23 / 44	**3.5**	**1.6-7.8**
		>1-5	10 / 14	**5.8**	**2.0-17**
		>5-10	9 / 19	**3.7**	**1.3-11**
		>10-15	3 / 8	2.0	0.4-9.4
		>15-20	1 / 2	2.9	0.2-39
		>20-25	0 / 0	--	
		> 25	0 / 0	--	
	Digital only	>1	427 / 1001	**1.7**	**1.01-22.7**
		>1-5	32 / 61	**2.7**	**1.4-5.3**
		>5-10	162 / 370	**1.7**	**1.03-3.0**
		>10-15	163 / 418	1.3	0.88-2.2
		>15-20	68 / 140	**1.9**	**1.1-3.4**
		>20-25	2 / 12	0.6	0.1-2.7
		> 25	0 / 0	--	
Hardell & Carlberg (2015)[18]	Analogue	>1	299 / 558	**1.6**	**1.2-2.0**
		>1-5	34 / 87	1.1	0.7-1.7
		>5-10	56 / 137	1.1	0.8-1.6
		>10-15	71 / 113	**2.2**	**1.5-3.2**
		>15-20	59 / 107	**2.4**	**1.5-3.7**
		>20-25	50 / 81	**3.2**	**1.9-5.5**
		> 25	29 / 33	**4.8**	**2.5-9.1**
	GSM	>1	884 / 2014	**1.3**	**1.1-1.6**
		>1-5	283 / 714	1.2	0.99-1.5
		>5-10	314 / 659	**1.7**	**1.3-2.2**
		>10-15	189 / 471	**1.4**	**1.04-1.9**
		>15-20	98 / 170	**2.1**	**1.5-3.0**
		>20-25	0 / 0	--	
		> 25	0 / 0	--	

UMTS	>1	58 / 141	2.0	0.95-4.4
	>1-5	46 / 127	1.9	0.9-4.1
	>5-10	12 / 14	**4.1**	**1.3-2.1**
	>10-15	0 / 0	--	
	>15-20	0 / 0	--	
	>20-25	0 / 0	--	
	> 25	0 / 0	--	
Mobile phone, total	>1	945 / 2148	**1.3**	**1.1-1.6**
	>1-5	262 / 674	1.2	0.98-1.5
	>5-10	301 / 688	**1.5**	**1.2-11.8**
	>10-15	211 / 476	**1.4**	**1.1-1.9**
	>15-20	92 / 196	**1.6**	**1.1-2.2**
	>20-25	50 / 81	**2.1**	**1.3-2.2**
	> 25	29 / 33	**3.0**	**1.7-5.2**
Mobile phone, digital (GSM + UMTS)	>1	885 / 2019	**1.3**	**1.1-1.6**
	>1-5	284 / 719	1.2	0.99-1.5
	>5-10	314 / 659	**1.7**	**1.3-2.2**
	>10-15	189 / 471	**1.4**	**1.04-1.9**
	>15-20	98 / 170	**2.1**	**1.5-3.0**
	>20-25	0 / 0	--	
	> 25	0 / 0	--	
Cordless	>1	752 / 1724	**1.4**	**1.1-1.7**
	>1-5	271 / 653	**1.3**	**1.1-1.6**
	>5-10	294 / 655	**1.4**	**1.1-1.8**
	>10-15	131 / 294	**1.4**	**1.1-1.9**
	>15-20	50 / 109	**1.7**	**1.1-2.5**
	>20-25	6 / 13	1.4	0.5-3.8
	> 25	0 / 0	--	
Digital (GSM + UMTS + cordless)	>1	1037 / 2393	**1.3**	**1.1-1.6**
	>1-5	295 / 796	1.2	0.9-1.4
	>5-10	363 / 758	**1.6**	**1.3-2.0**
	>10-15	242 / 584	**1.4**	**1.1-1.9**
	>15-20	131 / 242	**2.0**	**1.5-2.8**
	>20-25	6 / 13	1.6	0.6-4.4
	> 25	0 / 0	--	
All wireless	>1	1074 / 2472	**1.3**	**1.1-1.6**
	>1-5	271 / 748	1.1	0.9-1.4
	>5-10	351 / 767	**1.5**	**1.2-1.9**
	>10-15	248 / 578	**1.4**	**1.1-1.8**
	>15-20	121 / 253	**1.7**	**1.2-2.3**
	>20-25	54 / 93	**1.9**	**1.3-2.9**
	> 25	29 / 33	**3.0**	**1.7-5.2**

Abbreviations used:
Ca / Co: numbers of cases and controls; RR: relative risk; OR: odds ratio; CI: confidence interval.

Table D2 Glioma and cumulative call time.

Reference	Type of phone	Exposure			
Cohort study		Use	Ca	RR	95%CI
Benson et al. (2013)[12]	All mobile phone	Daily	36 (571 total)	0.80	0.56-1.14
		Ever	334 (571 total)	0.91	0.76-1.08
Case-control studies		Cumulative call time (h)	Ca / Co	OR	95%CI
Hardell et al. (2013) [17]	Analogue	>39-405	90 / 184	1.7	0.9-3.0
		406-1091	22 / 47	1.6	0.8-3.4
		1092-2376	18 / 23	**2.6**	**1.2-6.0**
		>2376	14 / 6	**7.7**	**2.5-24**
	GSM	>39-405	202 / 620	1.4	0.8-2.3
		406-1091	138 / 260	**1.9**	**1.1-3.3**
		1092-2376	84 / 199	1.4	0.8-2.5
		>2376	122 / 129	**3.2**	**1.8-5.6**
	UMTS	>39-405	35 / 87	1.1	0.5-2.4
		406-1091	16 / 34	1.0	0.4-2.6
		1092-2376	11 / 17	1.7	0.6-4.8
		>2376	5 / 2	5.1	0.8-32
	All mobile phone	>39-405	190 / 587	1.4	0.8-2.3
		406-1091	126 / 261	**1.7**	**1.02-3.0**
		1092-2376	95 / 210	1.5	0.9-2.7
		>2376	137 / 159	**2.8**	**1.6-4.8**
	Cordless	>39-405	164 / 434	1.3	0.8-2.2
		406-1091	120 / 278	**1.7**	**1.01-3.0**
		1092-2376	98 / 194	**2.1**	**1.2-3.7**
		>2376	79 / 109	**3.1**	**1.8-5.5**
	Digital (GSM +	>39-405	113 / 327	1.5	0.9-2.5
	UMTS + cordless)	406-1091	113 / 320	1.4	0.8-2.4
		1092-2376	139 / 317	**1.7**	**1.01-2.9**
		>2376	206 / 297	**2.6**	**1.5-4.3**
	All wireless	>39-405	108 / 317	1.5	0.9-2.5
	(mobile + cordless)	406-1091	110 / 314	1.4	0.8-2.4
		1092-2376	137 / 315	**1.7**	**1.003-2.9**
		>2376	216 / 315	**2.5**	**1.5-4.2**
Hardell & Carlberg (2015)[18]	Analogue	1-122	119 / 304	1.2	0.9-1.6
		123-511	88 / 146	**1.8**	**1.3-2.5**
		512-1486	50 / 82	**1.8**	**1.2-2.8**
		>1486	42 / 26	**4.8**	**2.8-8.2**
	GSM	1-122	328 / 885	**1.3**	**1.1-1.6**
		123-511	187 / 467	**1.3**	**1.01-1.7**
		512-1486	174 / 388	**1.5**	**1.1-1.9**
		>1486	195 / 274	**2.3**	**1.7-3.1**

UMTS	1-122	16 / 47	1.8	0.7-4.5
	123-511	17 / 54	1.5	0.6-3.8
	512-1486	20 / 31	**3.0**	**1.2-7.5**
	>1486	5 / 9	2.7	0.7-10
All mobile phone	1-122	340 / 920	**1.3**	**1.05-1.5**
	123-511	198 / 492	**1.3**	**1.02-1.6**
	512-1486	179 / 416	**1.4**	**1.04-1.8**
	>1486	228 / 320	**2.2**	**1.7-2.9**
Cordless	1-122	174 / 478	1.1	0.9-1.4
	123-511	203 / 534	1.2	0.97-1.6
	512-1486	210 / 451	**1.6**	**1.3-2.1**
	>1486	165 / 261	**2.3**	**1.8-3.1**
Digital (GSM + UMTS + cordless)	1-122	214 / 618	1.2	0.9-1.4
	123-511	232 / 583	**1.3**	**1.1-1.6**
	512-1486	241 / 613	**1.4**	**1.1-1.7**
	>1486	350 / 579	**2.1**	**1.7-2.7**
All wireless (mobile + cordless)	1-122	223 / 641	1.2	0.9-1.4
	123-511	235 / 596	**1.3**	**1.04-1.6**
	512-1486	249 / 617	**1.4**	**1.1-1.7**
	>1486	367 / 618	**2.0**	**1.6-2.6**

Table D3 Glioma and laterality.

Reference	Exposure / type of phone	Ipsilateral			Contralateral		
		Ca / Co	OR	95%CI	Ca / Co	OR	95%CI
Hardell et al. (2013)[17]	Ever use						
	Analogue	84 / 118	**2.3**	**1.2-4.5**	46 / 84	1.4	0.7-2.9
	GSM	322 / 530	**1.7**	**1.02-2.9**	190 / 404	1.4	0.8-2.5
	UMTS	38 / 69	1.2	0.5-2.8	24 / 45	1.1	0.4-3.1
	All mobile phone	324 / 534	**1.7**	**1.01-2.9**	190 / 407	1.4	0.8-2.5
	Cordless	272 / 454	**1.9**	**1.1-3.2**	156 / 327	1.6	0.9-2.8
Hardell & Carlberg (2015)[18]	Ever use						
	Analogue	190 / 252	**2.0**	**1.5-2.7**	98 / 184	1.3	0.9-1.9
	GSM	550 / 865	**1.8**	**1.4-2.2**	298 / 684	1.1	0.8-1.4
	UMTS	35 / 70	2.3	0.99-5.4	21 / 45	1.9	0.7-4.8
	All mobile phone	592 / 920	**1.8**	**1.4-2.2**	316 / 729	1.1	0.8-1.4
	Cordless	461 / 766	**1.7**	**1.3-2.1**	295 / 565	1.2	0.9-1.6

Time since 1st use (years)						
Mobile phone						
>1	592 / 920	**1.8**	**1.4-2.2**	316 / 729	1.1	0.8-1.4
>1-5	167 / 271	**1.6**	**1.3-2.1**	80 / 234	0.9	0.7-1.2
>5-10	187 / 289	**1.9**	**1.4-2.5**	106 / 238	1.3	0.9-1.8
>10-15	131 / 225	**1.7**	**1.2-2.3**	74 / 152	1.3	0.9-2.0
>15-20	59 / 84	**2.2**	**1.5-3.4**	29 / 76	1.0	0.6-1.7
>20-25	29 / 38	**2.3**	**1.3-4.1**	17 / 20	2.2	1.1-4.6
>25	19 / 13	**4.6**	**2.1-10**	10 / 9	3.2	1.2-8.6
Cordless phone						
>1	461 / 766	**1.7**	**1.3-2.1**	25 / 565	1.2	0.9-1.6
>1-5	161 / 292	**1.5**	**1.2-2.0**	98 / 205	1.3	0.9-1.7
>5-10	180 / 295	**1.8**	**1.3-3.4**	100 / 220	1..2	0.9-1.7
>10-15	82 / 126	**2.0**	**1.3-2.9**	46 / 99	1.2	0.8-1.9
>15-20	35 / 47	**2.6**	**1.5-4.4**	12 / 38	0.9	0.4-1.8
>20-25	3 / 6	1.4	0.3-5.9	3 / 3	1.9	0.4-10
>25	0 / 0	--		0 / 0	--	

Table D4 Glioma, analysis as continuous variables.

Reference	Variable	Type of phone	OR	95% CI
Hardell et al. (2013)[17]	Per 100 h of use	Analogue	**1.04**	**1.01-1.06**
		GSM	**1.01**	**1.01-1.02**
		UMTS	**1.03**	**0.99-1.08**
		All mobile phone	**1.01**	**1.01-1.02**
		Cordless phone	**1.01**	**1.01-1.02**
		Digital (GSM + UMTS + cordless)	**1.01**	**1.01-1.01**
		All wireless phone(mobile + cordless)	**1.01**	**1.01-1.01**
	Per year of use	Analogue	**1.04**	**1.02-1.07**
		GSM	**1.01**	**0.99-1.04**
		UMTS	1.04	0.89-1.22
		All mobile phone	1.02	0.99-1.03
		Cordless phone	1.01	0.99-1.04
		Digital (GSM + UMTS + cordless)	1.02	0.99-1.04
		All wireless phone(mobile + cordless)	**1.02**	**1.001-1.04**
Hardell & Carlberg (2015)[18]	Per 100 h of use	Analogue	**1.03**	**1.01-1.04**
		GSM	**1.01**	**1.01-1.01**
		UMTS	0.98	0.94-1.02
		Cordless	**1.01**	**1.01-1.02**
	Per year of use	Analogue	**1.06**	**1.04-1.08**
		GSM	**1.03**	**1.01-1.05**
		UMTS	1.13	0.96-1.33
		Cordless	**1.03**	**1.02-1.05**

Acoustic neuroma

Table D5 Acoustic neuroma and time since first use.

Reference	Type of phone	Exposure			
		Time since 1st use (years)			
Cohort study			Ca	RR	95%CI
Benson et al. (2013)[12]	All mobile phone	≥10	8 (96 total)	**2.46**	**1.07-5.64**
Case-control studies			Ca / Co	OR	95%CI
Hardell et al. (2013)[19]	Analogue	>1	86 / 558	**2.9**	**2.0-4.3**
		>1-5	16 / 87	**2.2**	**1.2-4.0**
		>5-10	33 / 137	**3.2**	**2.0-5.2**
		>10-15	16 / 113	**3.0**	**1.6-5.7**
		>15-20	9 / 107	**3.5**	**1.5-8.5**
		>20	12 / 114	**7.7**	**2.8-21**
	GSM	>1	173 / 2014	**1.5**	**1.1-2.1**
		>1-5	80 / 714	1.4	0.996-2.0
		>5-10	56 / 65	**1.8**	**1.1-2.8**
		>10-15	28 / 471	1.8	0.97-3.4
		>15-20	9 / 170	1.8	0.8-4.2
		>20	0 / 0	--	
	UMTS	>1	7 / 141	3.9	0.4-35
		>1-5	7 / 127	4.1	0.5-36
		>5-10	0 / 14	--	
		>10-15	0 / 0	--	
		>15-20	0 / 0	--	
		>20	0 / 0	--	
	All mobile phone	>1	200 / 2148	**1.6**	**1.2-2.2**
		>1-5	65 / 674	1.3	0.9-1.8
		>5-10	77 / 688	**2.3**	**1.6-3.3**
		>10-15	34 / 476	**2.1**	**1.3-3.5**
		>15-20	12 / 196	**2.1**	**1.02-4.2**
		>20	12 / 114	**4.5**	**2.1-9.5**
	Cordless	>1	156 / 1724	**1.5**	**1.1-2.1**
		>1-5	72 / 653	**1.5**	**1.05-2.1**
		>5-10	60 / 655	**1.6**	**1.1-2.5**
		>10-15	19 / 294	1.4	0.8-2.6
		>15-20	2 / 109	0.5	0.1-2.1
		>20	3 / 13	**6.5**	**1.7-26**
	Digital (GSM + UMTS + cordless)	>1	216 / 2393	**1.5**	**1.1-2.0**
		>1-5	93 / 796	**1.4**	**1.01-1.9**
		>5-10	73 / 758	**1.6**	**1.1-2.3**
		>10-15	38 / 584	1.6	0.97-2.8
		>15-20	9 / 242	1.1	0.5-2.5
		>20	3 / 13	**8.1**	**2.0-32**

	All wireless (mobile + cordless)	>1	227 / 2472	**1.5**	**1.1-2.0**
		>1-5	72 / 748	1.2	0.8-1.6
		>5-10	84 / 767	**1.9**	**1.3-2.7**
		>10-15	44 / 578	**2.0**	**1.3-3.2**
		>15-20	13 / 253	1.7	0.9-3.3
		>20	14 / 126	**4.4**	**2.2-9.0**
Corona et al. (2012)[34]	Analogue	0	26 / 69	1.00	
		<6	15 / 32	1.24	0.58-2.66
		≥6	3 / 3	2.65	0.50-13.99
	Digital	0	11 / 31	1.00	
		<6	15 / 38	1.11	0.45-2.77
		≥6	18 / 35	1.45	0.59-3.54
	All mobile phone	0	9 / 29	1.00	
		<6	12 / 34	1.14	0.42-3.08
		≥6	23 / 41	1.81	0.73-4.47
Moon et al. (2014)[35]	Mobile phone	Ca: 10.15±5.39 Co: 10.95±4.57	119 / 238	0.96	0.91-1.01
Petterson et al. (2014)[36]	Analogue	<5	6 / 3	2.85	0.7-11.6
		5-9	15 / 12	1.83	0.76-4.38
		≥10	36 / 44	1.17	0.66-2.08
	Digital	<5	51 / 77	1.14	0.73-1.78
		5-9	89 / 101	**1.53**	**1.02-2.32**
		≥10	68 / 103	1.13	0.74-1.73
	All mobile phone	<5	80 / 130	1.04	0.72-1.52
		5-9	119 / 150	1.40	0.98-2.00
		≥10	103 / 162	1.11	0.76-1.61
		10-12	42 / 67	1.10	0.68-1.76
		≥13	61 / 95	1.12	0.72-1.73
	Cordless	<5	110 / 165	1.29	0.92-1.81
		5-9	117 / 129	**1.72**	**1.21-2.45**
		≥10	66 / 109	1.22	0.82-1.80

Table D6 Acoustic neuroma and cumulative call time.

Reference	Type of phone	Exposure	Ca / Co	OR	95%CI
		Cumulative call time (h)			
Hardell et al. (2013)[19]	Analogue	1-122	42 / 304	**2.5**	**1.6-3.9**
		123-511	23 / 146	**3.1**	**1.8-5.5**
		512-1486	14 / 82	**4.2**	**2.1-8.4**
		>1486	7 / 26	**6.6**	**2.6-17**
	GSM	1-122	83 / 885	**1.5**	**1.04-2.1**
		123-511	30 / 467	1.2	0.7-2.0
		512-1486	38 / 388	**2.2**	**1.3-3.6**
		>1486	22 / 274	**2.1**	**1.2-3.9**
	UMTS	1-122	5 / 47	9.1	0.9-89
		123-511	1 / 54	1.5	0.1-26
		512-1486	1 / 31	2.7	0.2-47
		>1486	0 / 9	--	
	All mobile phone	1-122	91 / 920	**1.6**	**1.1-2.2**
		123-511	37 / 492	1.5	0.9-2.3
		512-1486	42 / 146	**2.4**	**1.5-3.8**
		>1486	30 / 320	**2.6**	**1.5-4.4**
	Cordless	1-122	36 / 478	1.2	0.8-1.8
		123-511	49 / 583	**1.6**	**1.03-2.3**
		512-1486	47 / 451	**2.1**	**1.3-3.2**
		>1486	24 / 261	**1.9**	**1.1-3.2**
	Digital (GSM + UMTS + cordless)	1-122	59 - 618	1.3	0.9-1.9
		123-511	49 / 583	1.3	0.9-2.0
		512-1486	58 / 613	**1.9**	**1.3-2.8**
		>1486	50 / 579	**2.1**	**1.4-3.3**
	All wireless (mobile + cordless)	1-122	57 / 641	1.2	0.8-1.7
		123-511	56 / 596	**1.5**	**1.02-2.2**
		512-1486	58 / 617	**1.9**	**1.3-2.8**
		>1486	56 / 618	**2.2**	**1.5-3.4**
Moon et al. (2014)[35]	All mobile phone	Ca: 1779±2496 Co: 2236±2533	119 / 238	0.96	0.91-1.01
Petterson et al. (2014)[36]	All mobile phone	<38	70 / 109	1.09	0.73-1.62
		38-189	73 / 109	1.12	0.74-1.69
		190-679	66 / 107	1.13	0.75-1.70
		>680	89 / 110	1.46	0.98-2.17
	Cordless	<84	64 / 96	1.22	0.82-1.82
		84-285	64 / 95	1.27	0.85-1.89
		285-900	70 / 97	1.42	0.96-2.09
		>900	84 / 97	**1.67**	**1.13-2.49**

Table D7 Acoustic neuroma and laterality.

Reference	Exposure / type of phone	Ipsilateral			Contralateral		
		Ca / Co	OR	95%CI	Ca / Co	OR	95%CI
Hardell et al. (2013)[19]	Ever use						
	Analogue	54 / 252	2.9	1.9-4.6	29 / 184	2.5	1.4-4.2
	GSM	108 / 865	1.7	1.1-2.4	62 / 684	1.3	0.9-2.1
	UMTS	3 / 70	1.9	0.2-20	3 / 45	3.6	0.3-38
	All mobile phone	123 / 920	1.8	1.3-22.6	73 / 729	1.5	0.9-2.2
	Cordless	101 / 766	1.8	12.-2.6	52 / 565	1.2	0.7-1.8
Corona et al. (2012)[34]	All mobile phone	14 / 26	1.40	0.65-3.04	7 / 26	0.57	0.23-1.43
Petterson et al. (2014)[36]	Analogue						
	Frequency of use						
	Never / rarely	84 / 108	1.00		76 / 96	1.00	
	Regular	34 / 30	1.43	0.79-2.58	23 / 22	1.44	0.69-3.00
	Digital						
	Frequency of use						
	Never / rarely	100 / 132	1.00		95 / 132	1.00	
	Regular	85 / 99	1.15	0.76-1.74	95 / 107	1.35	0.86-2.12
	All mobile phone						
	Frequency of use						
	Never / rarely	110 / 143	1.00		98 / 144	1.00	
	Regular	117 / 156	0.98	0.68-1.43	131 / 154	1.33	0.89-1.99
	Time since 1st use (years)						
	<5	39 / 51	1.05	0.62-1.78	35 / 41	1.41	0.80-2.48
	5-9	38 / 53	0.95	0.57-1.58	57 / 57	1.51	0.92-2.49
	≥10	40 / 51	1.01	0.61-1.68	39 / 56	1.09	0.63-1.88
	Cumulative call time (h)						
	<38	26 / 44	0.78	0.45-1.38	35 / 33	1.69	0.94-3.05
	38-189	28 / 32	1.18	0.63-2.20	30 / 41	1.05	0.56-1.95
	190-679	24 / 35	0.98	0.52-1.84	31 / 38	1.31	0.74-2.32
	≥680	38 / 43	1.20	0.69-2.08	33 / 39	1.26	0.70-2.25
	Cumulative no of calls						
	<1100	27 / 41	0.88	0.50-1.55	36 / 39	1.42	0.82-2.47
	1100-4400	31 / 31	1.44	0.76-2.74	27 / 31	1.31	0.70-2.44
	4400-13850	28 / 42	0.86	0.48-1.51	35 / 43	1.26	0.73-2.18
	≥13850	29 / 39	1.06	0.60-1.90	31 / 38	1.30	0.70-2.41

Table D8 Acoustic neuroma, analysis as continuous variables.

Reference	Variable	Type of phone				
Hardell et al. (2013)[19]	Incidence			OR	95% CI	
	Per 100 h of use	Analogue		**1.05**	**1.02-1.08**	
		GSM		1.01	0.99-1.02	
		UMTS		0.92	0.72-1.16	
		All mobile phone		**1.01**	**1.001-1.02**	
		Cordless phone		1.01	0.99-1.012	
		Digital (GSM + UMTS + cordless)		**1.01**	**1.0001-1.01**	
		All wireless phone(mobile + cordless)		**1.01**	**1.002-1.01**	
	Per year of use	Analogue		**1.10**	**1.06-1.14**	
		GSM		1.04	0.99-1.09	
		UMTS		0.99	0.67-1.47	
		All mobile phone		**1.06**	**1.03-1.09**	
		Cordless phone		1.03	0.99-1.07	
		Digital (GSM + UMTS + cordless)		**1.04**	**1.0003-1.07**	
		All wireless phone(mobile + cordless)		**1.06**	**1.03-1.09**	
	% change in tumour volume		n	% change	95% CI	p
	Per 100 h of use	Analogue	61	**+7.4**	**+1.0 to +14.2**	**0.02**
		GSM	116	+2.1	-4.1 to +8.6	0.52
		UMTS	7	--	--	--
		All mobile phone	137	+3.6	-1.1 to +8.6	0.13
		Cordless phone	104	+4.2	-3.8 to +13.0	0.31
		All wireless phone (mobile + cordless)	153	+3.6	-1.1 to +8.6	0.13
	Per year of use	Analogue	61	**+10.3**	**+2.4 to 18.7**	**0.01**
		GSM	116	+1.4	-0.6 to +3.5	0.18
		UMTS	7	--	--	--
		All mobile phone	137	+1.7	-0.1 to +3.5	0.06
		Cordless phone	104	+1.2	-1.1 to +3.6	0.31
		All wireless phone(mobile + cordless)	153	+1.0	-0.1 to +2.2	0.08

Table D9 Acoustic neuroma: tumour volume in case-case study.

Reference		Tumour volume (cm^3)	p
Moon et al. (2014)[35]	Use		
	Non-regular	2.71±3.78	
	Regular	8.10±10.71	**0.004**
	Time since 1st use (year)		
	≤10	5.57±8.15	
	>10	9.83±11.97	0.130
	Time of use per day (min)		
	≤20	4.88±5.60	
	>20	11.32±15.43	**0.026**
	Cumulative use (h)		
	≤2000	4.88±6.16	
	>2000	13.31±1.07	**0.007**

Meningioma

Table D10 Meningioma and time since first use.

Reference	Type of phone	Exposure			
		Time since 1st use (years)			
Cohort study			Ca	RR	95%CI
Benson et al. (2013)[12]	All mobile phone	≥10	20 (251 total)	1.10	0.66-1.84
Case-control studies			Ca / Co	OR	95%CI
Carlberg et al. (2013)[20]	Analogue	>1	108 / 260	0.9	0.6-1.5
		>1-5	0 / 0	--	
		>5-10	3 / 10	0.5	0.1-2.1
		>10-15	21 / 151	0.8	0.4-1.6
		>15-20	39 / 86	1.1	0.6-1.9
		>20-25	29 / 80	0.9	0.5-1.5
		>25	16 / 33	1.3	0.6-2.8
	GSM	>1	593 / 1208	1.0	0.7-1.4
		>1-5	70 / 109	1.1	0.7-1.7
		>5-10	236 / 477	0.9	0.7-1.4
		>10-15	212 / 453	1.0	0.7-1.5
		>15-20	75 / 169	1.0	0.6-1.5
		>20-25	0 / 0	--	
		>25	0 / 0	--	
	UMTS	>1	47 / 140	0.7	0.4-1.2
		>1-5	40 / 126	0.6	0.3-1.2
		>5-10	7 / 14	1.1	0.4-3.5
		>10-15	0 / 0	--	
		>15-20	0 / 0	--	
		>20-25	0 / 0	--	
		>25	0 / 0	--	

All mobile phone	>1	594 / 1217	1.0	0.7-1.4
	>1-5	69 / 108	1.1	0.7-1.7
	>5-10	217 / 423	1.0	0.7-1.4
	>10-15	185 / 399	1.0	0.7-1.4
	>15-20	78 / 174	1.0	0.6-1.5
	>20-25	29 / 80	0.8	0.5-1.4
	>25	16 / 33	1.2	0.6-2.3
Cordless	>1	522 / 10115	1.1	0.8-1.5
	>1-5	109 / 209	1.0	0.7-1.5
	>5-10	217 / 436	1.0	0.7-1.5
	>10-15	128 / 248	1.1	0.8-1.7
	>15-20	61 / 109	1.2	0.7-1.8
	>20-25	7 / 13	1.3	0.5-3.4
	>25	0 / 0	--	
Digital (GSM + UMTS + cordless)	>1	641 / 1261	1.0	0.7-1.5
	>1-5	43 / 64	1.2	0.7-1.9
	>5-10	222 / 420	1.0	0.7-1.4
	>10-15	248 / 523	1.0	0.7-1.54
	>15-20	121 / 241	1.1	0.7-1.6
	>20-25	7 / 13	1.2	0.5-3.3
	>25	0 / 0	--	
All wireless (mobile + cordless)	>1	641 / 1261	1.0	0.7-1.5
	>1-5	42 / 61	1.2	0.7-2.0
	>5-10	206 / 378	1.0	0.7-1.5
	>10-15	226 / 466	1.0	0.7-1.5
	>15-20	115 / 231	1.1	0.7-1.6
	>20-25	36 / 92	0.9	0.5-1.5
	>25	16 / 33	1.2	0.6-2.4

Table D11 Meningioma and cumulative call time.

Reference	Type of phone	Exposure	Ca / Co	OR	95%CI
		Cumulative call time (h)			
Carlberg et al. (2013)[20]	Analogue	>39-405	77 / 184	0.9	0.6-1.5
		406-1091	12 / 47	0.6	0.3-1.4
		1092-2376	12 / 23	1.3	0.6-2.9
		>2376	7 / 6	3.0	0.9-9.7
	GSM	>39-405	317 / 620	1.0	0.7-1.4
		406-1091	122 / 260	1.0	0.7-1.5
		1092-2376	75 / 199	0.9	0.6-1.4
		>2376	79 / 129	1.5	0.9-2.3
	UMTS	>39-405	30 / 87	0.7	0.3-1.3
		406-1091	6 / 34	0.4	0.1-1.2
		1092-2376	6 / 17	0.6	0.2-1.8
		>2376	5 / 2	7.3	1.2-4.6

All mobile phone	>39-405	306 / 587	1.0	0.7-1.4
	406-1091	119 / 261	1.0	0.7-1.4
	1092-2376	85 / 210	0.9	0.6-1.4
	>2376	84 / 159	1.3	0.8-1.9
Cordless	>39-405	194 / 434	1.0	0.7-1.4
	406-1091	116 / 278	0.9	0.6-1.3
	1092-2376	117 / 194	1.2	0.8-1.8
	>2376	95 / 109	1.8	1.2-2.8
Digital (GSM + UMTS + cordless)	>39-405	185 / 327	1.1	0.8-1.6
	406-1091	134 / 320	0.9	0.6-1.3
	1092-2376	135 / 317	0.9	0.6-1.3
	>2376	187 / 297	1.4	0.96-2.0
All wireless (mobile + cordless)	>39-405	178 / 317	1.1	0.7-1.5
	406-1091	134 / 314	0.9	0.6-1.3
	1092-2376	138 / 315	0.9	0.6-1.4
	>2376	191 / 315	1.4	0.9-2.0

Table D12 Meningioma and laterality.

Reference	Exposure / type of phone	Ipsilateral			Contralateral		
		Ca / Co	OR	95%CI	Ca / Co	OR	95%CI
Carlberg et al. (2013)[20]	Ever use						
	Analogue	54 / 118	1.4	0.8-2.4	42 / 84	1.2	0.6-2.2
	GSM	283 / 530	1.1	0.7-1.6	214 / 404	1.1	0.7-1.6
	UMTS	26 / 69	0.8	0.4-1.8	17 / 45	0.8	0.3-2.1
	All mobile phone	284 / 534	1.1	0.7-1.6	214 / 407	1.1	0.7-1.6
	Cordless	244 / 454	1.1	0.7-1.6	188 / 327	1.2	0.8-1.8

Table D13 Meningioma, analysis as continuous variables.

Reference	Variable	Type of phone				
Carlberg et al. (2013)[20]	Incidence				OR	95% CI
	Per 100 h of use	Analogue			1.02	1.0004-1.04
		GSM			1.01	0.99-1.01
		UMTS			1.04	1.0002-1.07
		All mobile phone			1.01	1.001-1.01
		Cordless phone			1.01	1.01-1.02
		Digital (GSM + UMTS + cordless)			1.01	1.003-1.01
		All wireless phone (mobile + cordless)			1.01	1.003-1.01
	Per year of use	Analogue			1.00	0.98-1.03
		GSM			0.99	0.98-1.02
		UMTS			0.93	0.80-1.08
		All mobile phone			0.99	0.98-1.01
		Cordless phone			1.01	0.99-1.03
		Digital (GSM + UMTS + cordless)			1.00	0.98-1.02
		All wireless phone (mobile + cordless)			1.00	0.98-1.02
	% change in tumour volume					
			n	% change	95% CI	p
	Per 100 h of use	Analogue	98	+1.6	-4.7 to +8.3	0.62
		GSM	530	-0.9	-4.0 to +2.2	0.56
		UMTS	41	+9.6	-21.1 to +52.4	0.57
		All mobile phone	531	-0.5	-2.8 to +1.9	0.68
		Cordless phone	465	-0.8	-3.6 to +2.0	0.57
		All wireless phone (mobile + cordless)	570	-0.2	-2.5 to +2.1	0.86
	Per year of use	Analogue	98	+0.1	-2.0 to +2.2	0.96
		GSM	530	+0.1	-0.6 to +0.8	0.83
		UMTS	41	+1.3	-2.0 to +4.7	0.42
		All mobile phone	531	+0.1	-0.5 to +0.1	0.84
		Cordless phone	465	-0.3	-0.7 to +0.1	0.13
		All wireless phone (mobile + cordless)	570	-0.2	-0.5 to +0.1	0.19

Pituitary tumour

Table D14 Pituitary tumour and time since first use.

Reference	Type of phone	Exposure			
		Time since 1st use (years)			
Cohort study			Ca	RR	95% CI
Benson et al. (2013)[12]	All mobile phone	≥10	11 (110 total)	1.61	0.78-3.35

Health Council of the Netherlands

Advisory Reports

The Health Council's task is to advise ministers and parliament on issues in the field of public health. Most of the advisory opinions that the Council produces every year are prepared at the request of one of the ministers.

In addition, the Health Council issues unsolicited advice that has an 'alerting' function. In some cases, such an alerting report leads to a minister requesting further advice on the subject.

Areas of activity

Optimum healthcare
What is the optimum result of cure and care in view of the risks and opportunities?

Prevention
Which forms of prevention can help realise significant health benefits?

Healthy nutrition
Which foods promote good health and which carry certain health risks?

Environmental health
Which environmental influences could have a positive or negative effect on health?

Healthy working conditions
How can employees be protected against working conditions that could harm their health?

Innovation and the knowledge infrastructure
Before we can harvest knowledge in the field of healthcare, we first need to ensure that the right seeds are sown.

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