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Review

Estimating the risk of brain tumors from cellphone use: Published case–control studies

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Abstract

This paper reviews the results of early cellphone studies, where exposure duration was too short to expect tumorigenesis, as well as two sets of more recent studies with longer exposure duration: the Interphone studies and the Swedish studies led by Dr. Lennart Hardell. The recent studies reach very different conclusions. With four exceptions the industry-funded Interphone studies found no increased risk of brain tumors from cellphone use, while the Swedish studies, independent of industry funding, reported numerous findings of significant increased brain tumor risk from cellphone and cordless phone use. An analysis of the data from the Interphone studies suggests that either the use of a cellphone *protects* the user from a brain tumor, or the studies had serious design flaws. Eleven flaws are identified: (1) selection bias, (2) insufficient latency time, (3) definition of 'regular' cellphone user, (4) exclusion of young adults and children, (5) brain tumor risk from cellphones radiating higher power levels in rural areas were not investigated, (6) exposure to other transmitting sources are excluded, (7) exclusion of brain tumor types, (8) tumors outside the cellphone radiation plume are treated as exposed, (9) exclusion of brain tumor cases because of death or illness, (10) recall accuracy of cellphone use, and (11) funding bias. The Interphone studies have all 11 flaws, and the Swedish studies have 3 flaws (8, 9 and 10). The data from the Swedish studies are consistent with what would be expected if cellphone use were a risk for brain tumors, while the Interphone studies data are incredulous. If a risk does exist, the public health cost will be large. These are the circumstances where application of the Precautionary Principle is indicated, especially if low-cost options could reduce the absorbed cellphone radiation by several orders of magnitude.

Keywords: Electromagnetic field; Cellphone; Brain tumor; Mobile phone; Cellular phone; Cordless phone; Glioma; Acoustic neuroma; Meningioma; Funding; Interphone

Contents

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1. Introduction

This review covers all case–control studies on the risk of brain tumors from cellphone use published up to March 2009 and does not include epidemiological studies on the risk of brain tumors from exposure to other sources of electromagnetic fields (EMFs). It examines the strengths and weaknesses of these studies and what can be learned from differences in the findings. Because certainty is not possible in science, much less in epidemiology, the indication of a possible risk of brain tumors from cellphone use suggests that the Precautionary Principle be applied.

In almost all epidemiological investigations of rare diseases, such as brain tumors, researchers use what is known as a case–control design. Cases are subjects who have the disease and controls are randomly chosen subjects without the disease. Typically controls are matched to the cases by age, gender, geographical area, and income. Subjects are asked a set of questions, which for a cellphone study would include questions about their cellphone use.

The Odds Ratio (OR), the increased risk (OR > 1.0), or decreased risk (OR < 1.0) of brain tumors as a result of exposure to cellphone radiation is reported. A two-by-two table is used to calculate the Odds Ratio. In Table 1, Case and Control subjects are in the rows and Exposed and Unexposed subjects are in the columns. The Odds Ratio = (Exposed Cases) × (Unexposed Controls)/(Exposed Controls) × (Unexposed Cases).

Actual studies use sophisticated statistical regression analysis to adjust for confounding effects (age, gender, smoking, etc.), but the basic concept is the same. Additionally, along with the Odds Ratio, a 95% confidence interval (CI) is reported.

In this discussion cellphone studies are grouped into early studies and later studies. The later studies are presented as two sets of studies. Since each set uses a common protocol, each can be considered a single study: The two sets are the industry-funded Interphone studies and the independently funded Swedish studies led by Dr. Lennart Hardell.

2. Early case–control cellphone studies

The salient fact of these early studies is the short duration of cellphone use. It would have been surprising to find any risk of a brain tumor, because an increased risk would have required a short latency time between exposure and diagnosis. Indeed, none of these studies reported finding a significant risk ($p \leq 0.05$) of a brain tumor from cellphone use. Yet, as can be seen in Table 2, each study did find a non-significant ($p > 0.05$) increased risk including two near-significant findings of increased risk ($p < 0.10$). And, Auvinen et al. found that for each year of cellphone use a significant 20% increased risk of a brain cancer (glioma). Table 2 summarizes these studies [1–5].

Perhaps these early studies that found no significant risk had actually found an early warning of trouble ahead.

3. The industry-funded Interphone study

The Interphone study is a 13-country case–control study on the risk of brain and salivary gland tumors from cellphone use. The Interphone study uses a standard protocol such that all individual country results can be pooled together to increase the power of the study. This discussion is limited to the brain tumors studies.

As of December 2008 there have been 11 single-country and 3 multi-country Interphone brain tumor studies published [6–19]. The multi-country studies will not be discussed

Table 1
Simple example of increased risk.

	Exposed	Unexposed	Totals
Cases	60	40	100
Controls	49	51	100
Totals	109	91	200
Odds Ratio	1.56		

Table 2
Early cellphone case–control studies.

Study	Cases	Eligibility		Av. use time years	Major findings				Comments
		Start	End		OR	95% CI		p value	
Hardell et al., May 2000 [1]	209	1994–1996 (Uppsala-Orebro) 1995–1996 (Stockholm)		Not reported	2.42	0.97	6.05	0.053†	Temporal, parietal, occipital lobes—ipsilateral use (number of cases not reported)
Muscat et al., December 2000[a] [2]	469	1994	1998	2.8	2.1	0.9	4.7	0.073†	Neuroepithelial cancer (35 cases)
Inskip et al., January 2001 [3]	782	June-94	August-98	Not reported	1.9	0.6	5.9	0.26	Acoustic neuroma, ≥5 years of use (5 cases)
Muscat et al., May 2002[a] [4]	90	1997	1999	4.1	1.7	0.5	5.1	0.36	Acoustic neuroma, 3–6 years of use (11 cases)
Auvinen et al., May 2002[a] [5]	398		1996	Av. 2–3 (analog) <1 (digital)	1.7	0.9	3.5	0.12	Glioma, >2 years of use (number of cases not reported)
					1.2	1.0	1.4	0.050	Glioma, increase risk per year (number of cases not reported)

Bold indicates statistically significant ($p \leq 0.05$).
[a] Industry funded study.
† Near-significant ($p \leq 0.10$).

Table 3
Summary data of the 11 Interphone studies investigated.

Study, Country	Tumor	Dx eligibility range years	% Cases ≥10 years	% of eligible controls refusing participation	"Regular" use from abstract	
					OR	CI
Lönn et al. 2004, Sweden	AN	3.0	9.5%	27.9%	1.0	0.6 to 1.5
Christensen et al. 2004, Denmark	AN	2.0	1.4%	36.0%	0.90	0.51 to 1.57
Lönn et al. 2005, Sweden	G M	2.0	6.7% 4.4%	29.5%	**0.8** **0.7**	0.6 to 1.0 0.5 to 0.9
Christensen et al. 2005, Denmark	L-g G H-g G M	2.0	5.6% 3.4%	36.0%	1.08 **0.58** 1.00	0.58 to 2.00 0.34 to 0.90 0.54 to 1.28
Schüz et al. 2006, Germany	G M	3.0	3.3% 1.3%	39.0%	0.98 0.84	0.74 to 1.29 0.62 to 1.13
Takebayashi et al. 2006, Japan	AN	3.9	8.2%	15.8%	0.73	0.43 to 1.23
Klaeboe et al. 2007, Norway	AN G M	2.0	0.0% 0.0% 0.0%	31.0%	**0.5** **0.6** 0.8	0.2 to 1.0 0.4 to 0.9 0.5 to 1.1
Hours et al. 2007, France	AN G M	2.5	0.0% 0.0% 0.0%	28.8%	0.92 1.15 0.74	0.53 to 1.59 0.65 to 2.05 0.43 to 1.28
Hepworth et al., 2007, United Kingdom	G	3.3	6.8%	65.5%	0.94	0.78 to 1.13
Schlehofer et al., 2007, Germany	AN	3.1	0.0%	45.1%	0.67	0.38 to 1.19
Takebayashi et al. 2008, Japan	G M	3.9	2.3% 4.5%	56.3% 12.9%	1.22 0.70	0.63 to 1.27 0.42 to 1.16
Weighted average (by cases)		**2.7**	**6.2%**	**40.7%**		
Wt. Av. (by cases) excluding Lönn (2004) and Hepworth		**2.7**	**6.2%**	**33.4%**		

AN = acoustic neuroma; G = glioma; M = meningioma; L-g G = low-grade glioma; H-g G = high-grade glioma. Bold OR indicates statistically significant protection.

further because they overlap the single-country studies [17–19]. Table 3 summarizes the 11 Interphone studies included in this analysis. Three studies had no cases who had used a cellphone for ≥10 years [12,14,16]. For Odds Ratios (ORs) on the risk of brain tumors from "regular" cellphone use (reported in the abstracts) there were 15 ORs <1.0—a protective result (4 with significant protection), and 2 ORs were >1.0—a result indicating increased risk. The cumulative binomial probability of having 15 ORs <1.0 and 2 ORs >1.0 is highly unlikely ($p = 0.0012$) and indicates a significant protective effect.

Table 3 summarizes the 11 Interphone studies analyzed in this paper. It shows the years available for case diagnosis (Dx) to be eligible for participation in the study, the percentage of cases that used a cellphone for 10 or more years, the percentage of selected controls that refused to participate in the study, and the Odds Ratios of brain tumors for "regular" cellphone use reported in the abstract of each paper. Finally, weighted (by cases) averages are presented for the Dx years for eligibility in the studies, the % of cases that used a cellphone for ≥10 years, and the % of eligible controls that refused participation.

All 14 of these Interphone brain tumor studies have found that use of a cellphone *protects* the user from a brain tumor. The 11 studies reported a total of 284 statistically independent ORs; 217 ORs <1.0 and 67 ORs >1.0 ($p = 6.2 \times 10^{-20}$). There are two possibilities to explain such an incredulous result: (1) Either use of a cellphone provides protection from a brain tumor, or (2) the Interphone Protocol [20] has serious design flaws.

Eleven design flaws have been identified. The consistent findings of protection can be explained because 8 of these 11 flaws underestimate the risk of brain tumors.

3.1. Flaw 1: selection bias

In a case–control cellphone study both cases and controls are asked if they would like to participate in the study. It is reasonable to assume controls who use a cellphone are more likely to participate than controls who do not use a cellphone. This would result in selection bias. And, such selection bias would result in an underestimation of risk.

The impact of selection bias increases as the percentage of controls that refuse to participate increases. The Interphone control weighted-average refusal rate was a remarkably high 41%. Dr. Sam Milham, an occupational epidemiologist with over 100 published papers, states that in the past, science journals would not accept a study with such a high refusal rate [21].

One Interphone study investigated the possibility of selection bias by asking controls that refused participation if they used a cellphone; 34% said they used a cellphone and 59% said they did not use a cellphone, confirming selection bias in that study [6].

How could selection bias have been mitigated? First, do not tell subjects the study is a cellphone study. Second, pay the subjects for participation in the study. The result would be a higher participation rate, and more importantly, control participation would not be biased for use, or non-use of a cellphone. However, given the funding provided, paying subjects was not considered.

Table 4
Odds Ratios, with and without selection bias.

	Exposed	Unexposed	Totals
With selection bias			
Cases	60	40	100
Controls	***60***	40	100
Totals	120	80	200
Odds Ratio	1.00		
	Truly Exposed	**Unexposed**	**Totals**
Without selection bias			
Cases	60	40	100
Controls	***49***	51	100
Totals	109	91	200
Odds Ratio	1.54		

Exposed Controls = (60 user "participating" controls) × (59% participation) + (34 cellphone users among non-participating controls) × (41% non-participants) = 49.

Table 4, using semi-hypothetical data (i.e., data that approximates actual Interphone data), illustrates how the Odds Ratios will change when selection bias exists and when the selection bias has been eliminated. As can be seen the Odds Ratio increases from 1.00 (no risk) to 1.54. Inversely stated, with selection bias a finding of no risk would mask an actual risk.

3.2. Flaw 2: insufficient latency time

The known latency time (the time between exposure and diagnosis) for brain tumors is 30+ years [22], similar to lung cancer from smoking [23] and mesothelioma from asbestos exposure [24]. Ten or more years was the longest cellphone use time reported. The weighted-average of brain tumors cases with ≥10 years of cellphone use was 6.2% of all cases, or 16 cases per study. Not including sufficient numbers of longer-term cellphone users results in an underestimation of risk.

To resolve this problem would require about a 3-fold increase in subjects. Because the weighted-average diagnosis eligibility time was only 2.7 years (the date range for cases to be diagnosed with a brain tumor to be eligible for the study), only a small number of subjects were available. There was insufficient funding to increase the eligibility time.

It is worth noting, two independently funded cellphone case–control studies, used a 6-year eligibility time. These two studies showed a consistent risk of brain tumors for ≥10 years of cellphone use [25,26].

3.3. Flaw 3: definition of “regular” cellphone user

The Interphone Protocol defines “regular” cellphone use as use for at least once a week for 6 months or more with any cellphone use 1 year prior to diagnosis excluded. Based on UK cellphone subscriber data [27] and the UK study’s Dx eligibility dates [13], the rapid rise of cellphone use finds 85% of “regular” UK users had used a cellphone for less than 5 years; 98% of “regular” UK users had used a cellphone for less than 10 years (all Interphone countries have similar rapid increases in cellphone users). Given known latency times how could any risk of brain tumors be expected for “regular” users? Inclusion of such a large proportion of short-term users underestimates the risk of brain tumors.

Dr. Elizabeth Cardis, the head of the Interphone study stated, “Reporting ‘regular’ user [data] was not intended to be a risk factor.” [28]. Yet, the abstract of every Interphone brain tumor study highlights that there is no risk of brain tumors from “regular” cellphone use.

3.4. Flaw 4: exclusion of young adults and children

The Interphone Protocol requires subjects to be between 30 and 59 years of age (some studies have included ages as low as 20). There is strong evidence that the young adults and children are at greater risk from exposure to carcinogens than mature adults suggesting that the young, with greater cell growth, are more vulnerable to genetic mutations.

Two cellphone studies report higher brain tumor risks in young adults (20–29 years of age) compared to mature adults. The first study found a 7-fold increased risk of brain tumor compared to a 1.40-fold risk for all adults [29], and the second study found a 3.2-fold risk of brain tumor [30] compared to <2-fold risk in older adults. An ionizing radiation brain tumor study found the younger a child’s age, the greater the risk of brain tumors (4.6-fold/Gy risk of brain tumors for children less than 5 years of age; 3.2-fold/Gy risk for children 5 to 9 years of age, and; 1.47-fold/Gy risk for children 10 or more years) [22].

Inclusion of additional cases below 30 years would have provided greater insight into risk, but the additional cases would have increased the cost of the study.

3.5. Flaw 5: brain tumor risk from cellphones radiating higher power levels in rural areas were not investigated

Because rural users are farther away from the cell towers compared to urban users, the cellphone’s radiated power is higher [31]. Unfortunately the Interphone studies selected mostly metropolitan areas to locate brain tumor cases. When higher radiated power is not included there is an underestimation of risk.

In order to have sufficient cases to achieve statistical power, the total number of cases and controls who live in rural areas would have to be increased. This would require additional funding compared to what was provided.

Table 5
Change in Odds Ratios cordless phone use is not included and when it is included.

	Exposed	Unexposed	Totals
Cordless phone exposure treated as unexposed			
Cases	***43***	57	100
Controls	***27***	73	100
Totals	70	130	200
Odds Ratio	2.0		

	Truly exposed	Unexposed	Totals
Cordless phone exposure treated as exposed			
Cases	***64***	36	100
Controls	***40***	60	100
Totals	104	96	200
Odds Ratio	2.6		

Truly Exposed Controls = (27 “Exposed” Controls) × (64 truly exposed cases/43 “Exposed” Cases) = 40.

3.6. Flaw 6: exposure to other transmitting sources are not considered

Subjects who use cordless phones, walkie-talkies, Ham radio transmitters, etc. are treated as unexposed in the Interphone study when in fact they are exposed. Again, it is important to note that two independently funded cellphone case–control studies treated cordless phone use as exposed, and found that cordless phone use results in an increased risk of brain tumors [25,26]. Treating exposed subjects as unexposed, once again, underestimates the risk of brain tumors.

Table 5 illustrates how the Odds Ratio would change if cordless phone users had been treated as exposed subjects. The first Odds Ratio table assumes a 2.0-fold risk. Additionally it assumes that 57% of cases did not use a cellphone (without considering cordless phone use). The second table assumes when cordless phone use is considered that the number of unexposed cases decreases to 36%. An additional assumption is cordless phones have the same risk of brain tumors as do cellphones. Given these assumptions we see that the inclusion of cordless phone use as an exposure increased the 2.0-fold risk to a 2.6-fold risk.

3.7. Flaw 7: exclusion of brain tumor types

The Interphone study includes three brain tumor types: acoustic neuroma, glioma and meningioma. Other types are excluded (e.g. brain lymphoma, neuroepithelial, etc.). Exclusion of these other tumors underestimates the risk of brain tumors.

Interestingly, as shown in Table 2 above, another industry-funded study reported a 2.1-fold risk of a neuroepithelial brain tumor [2] and an industry-funded cellphone study showed an excess risk of lymphoma in mice [32]. Given this knowledge it is surprising that all brain tumor types were not included.

3.8. Flaw 8: tumors outside the cellphone's radiation plume are treated as exposed

The radiation plume's volume is a small proportion of the brain's volume. Treating tumors outside the radiation plume as exposed tumors results in an overestimation of risk (the only flaw that overestimates risk).

The adult brain absorbs the cellphone's radiation almost entirely on the side of the head where the cellphone is held (ipsilateral); almost no radiation is deposited on the opposite side of the head (contralateral). In adults the ipsilateral temporal lobe absorbs 50–60% of the total radiation and is ~15% of the brain's volume. The ipsilateral cerebellum absorbs 12–25% of the total radiation and is ~5% of the brain's volume. Thus, 62–85% of the cellphone's radiation is absorbed by ~20% of an adult's brain's volume [33]. Because a child's brain absorbs far more radiation than an adult's brain, this data are not applicable for a child's brain.

Table 6, using semi-hypothetical data, shows how the Odds Ratio will change when all tumors are treated as exposed and when only tumors within the cellphone's radiation plume are treated as exposed. This hypothetical example assumes there is a 2.0-fold risk when all tumors are treated as exposed, and assumes that only 20% of the tumors are actually exposed. Per these assumptions, the apparent 2.0-fold risk is reduced to a 1.6-fold risk.

Because the proportion of all brain tumors to the tumors within the radiation plume is small, a larger (roughly 5-fold) number of subjects would be required. However, the funding provided, did not allow for such a large increase in subjects.

A recent paper showing changes in the brain's blood brain barrier (BBB) permeability reported, counter-intuitively, that the effect of the highest permeability of the BBB (highest leakage) occurs at lower exposures [34]. The effect of this phenomenon is that almost all the leakage from a GSM cellphone occurs deep in the brain and on the contralateral side.

Table 6
Odds Ratios with all tumors exposed and without all tumors exposed.

	Exposed	Unexposed	Totals
With flaw 8 design error			
Cases	75	25	100
Controls	60	40	100
Totals	135	65	200
Odds Ratio		2.0	
	Truly exposed	**Unexposed**	**Totals**
Without flaw 8 design error			
Cases	**15**	70	85
Controls	**12**	88	100
Totals	27	158	185
Odds Ratio		1.6	

Truly Exposed Cases = (75 "exposed" cases) × (20% brain exposed) = 15. Truly Exposed Controls = (60 "exposed" controls) × (20% brain exposed) = 12.

Whether this is similar for the induction of brain tumors is unknown. However, whether or not it is similar does not negate the fact that the cellphone's radiation plume is in a small proportion of the total brain's volume.

3.9. Flaw 9: exclusion of brain tumor cases because of death or too ill to respond

A large number of brain cancer (glioma) cases died before they could be interviewed or were too ill to be interviewed. Common practice would be to interview a proxy (e.g., a spouse). The Interphone Protocol requires use of proxies in case of death [20], yet 3 of the 7 glioma studies excluded deceased, or too ill to be interviewed cases from their studies [9,12,13] and a 4th did not use proxies for all of the cases who were too ill to be interviewed or who had died [10]. The weighted average of these exclusions was 23% of all glioma cases. This flaw limits determining the risks, if any, from the most deadly and debilitating brain tumors from cellphone use.

Another study found significant risks for high-grade glioma (the most deadly), but not for low-grade glioma (the least deadly) [35].

3.10. Flaw 10: recall accuracy of cellphone use

Memory accuracy, particular in the distant past, is limited at best. The Interphone project investigated this problem by asking cellphone users to recall their cellphone use, and then compared the recall to billing records.

The study reported that light cellphone users tend to underestimate their use and heavy users tend to overestimate their use. This results in an underestimation of risk [36].

Accurate data for the Interphone study could have been obtained by accessing subjects' cellphone-billing records as was done in the study of recall bias [36]. It is reasonable to assume that the available funding did not support the gathering of billing records.

3.11. Flaw 11: funding bias

If studies are funded by an entity with a financial interest in the findings, it has been shown that, more often than not, the findings of such a study are favorable to the financial interest compared to studies where the funding has no financial interest.

Dr. Henry Lai at Washington University in Seattle maintains a database of cellphone biological studies. The results (Table 7) from his database (July 2007) report the magnitude of funding bias. The industry-funded studies found an effect in 28% of the studies and the independently funded studies found an effect 67% of the time. The probability that this is a chance finding is extraordinarily minute ($p = 2.3 \times 10^{-9}$).

A study on the source of funding of cellphone studies and the reported results reported, "We found that the studies funded exclusively by industry were indeed substantially less likely to report statistically significant effects on a range of

Table 7
Industry-funded and independently funded cellphone biological studies.

		Cellphone biological studies					
		Effect found		No effect found		Studies	% all studies
		Studies	% all studies	Studies	% all studies		
Industry funded	No.	27	8.3%	69	21.2%	96	29.4%
	%	28.1%		71.9%			
Independently funded	No.	154	47.5%	76	23.5%	230	70.6%
	%	67.0%		33.0%			
Totals		181	55.5%	145	44.5%	326	100.0%

$\text{Chi}^2 = 39.8$ ($p = 2.3 \times 10^{-9}$) 11 July 2006.

end points that may be relevant to health" (probability of industry-funded study reporting at least one significant result is 0.11, CI: 0.02–0.78) [37].

Financial bias is pervasive across all fields of science. It is sufficiently pervasive that books have been written on the subject and science journals have brought it to the attention of their readers. A search for books about "Funding Bias in Science" at Amazon.com found 86 titles [38].

In a review of the book 'Science in the Private Interest: Has the Lure of Its Profits Corrupted Biomedical Research?' by Sheldon Krimsky, Dr. Roger Porter wrote, "The major theme of this superb book, therefore, is the degradation of the academic scientist, who is lured to the pecuniary gains offered by industry and now asks the scientific questions posed by industry instead of independently pursuing scientific investigation of public needs." [39].

A news report in the British Medical Journal reported, "Four German public health scientists have been publicly criticised in Der Spiegel magazine for accepting funding from the tobacco industry in return for supporting tobacco friendly research projects and policies in the 1980s." [40].

A substantial portion of the Interphone study funding comes from the cellphone industry. For European studies, industry has provided more than €3.2 million ($5.1M) [27], another $1 million came from the Canadian Wireless Telecommunications Association [41] and it is unknown if industry funding has been provided for studies in Japan, Australia and New Zealand.

In addition to the €3.2 million the Interphone Exposure Assessment Committee received funding from the UK Network Operators (O2, Orange, T-Mobile, Vodafone, '3') and French Network Operators (Orange, SFR, Bouygues) [36]. At least one member of this Committee is employed by a cellphone company: Dr. Joe Wiart from France Telecom [20].

Beyond the €3.2 million available to the European Interphone studies, the French study [12] received funding from "Orange, SFR, Bouygues Télécom." [42]; the UK study received funding from O2, Orange, T-Mobile, and Vodafone, and [13]; the Danish study received funds from the for-profit International Epidemiology Institute (IEI). The source of the IEI funds is not stated [9].

Funding for the 5-country Interphone study of acoustic neuroma also came from O2, Orange, T-Mobile, Vodafone, '3' [18].

The Muscat et al. studies [2,4] received around $600,000 from the Cellular Telecommunication Industry Association (CTIA) via the organization CTIA created and funded, Wireless Technology Research (WTR) [43]. For the Auvinen et al. study "Finnish mobile phone manufacturers contributed to the funding for the TEKES research program." [5].

4. Increased risk Interphone laterality findings

So far the discussion had pertained to the aggregate results of the 11 Interphone brain tumor studies. It is important to note that when significant findings of risk were examined for ≥10 years of cellphone use it was found that 2 studies had 3 significantly increased risk results (all 3 were for ipsilateral use). The Swedish Lönn et al. acoustic neuroma study had two significant results showing an increased risk: OR = 3.9 (CI: 1.6 to 9.5) for ≥10 years since first ipsilateral use (based on 12 cases), and OR = 3.1 (CI: 1.2 to 8.4) for ≥10 years of ipsilateral use (based on 9 cases) [6]. The UK Hepworth et al. glioma study reported OR = 1.24 (CI: 1.02 to 1.52) for ≥10 years of ipsilateral use (based on 278 cases) [13].

If we examine Table 3 there is little difference between the parameters of these studies relative to the weighted average of all 11 studies. The Lönn et al. acoustic neuroma study had the third smallest control refusal rate (27.9%), yet the Hepworth et al. glioma study had the highest control refusal rate (65.5%).

When the weighted averages are calculated without the Lönn (2005) and Hepworth studies (see Table 3) the Dx years and the % of cases who used a cellphone for >10 years remained unchanged. However, the % of controls who refused to participate is 33.4% (from 40.7%). This is because the Hepworth study has the hightest number of controls of any of the 11 studies (1716 controls, 24% of all controls) and the highest control refusal rate (65.5%) of the 11 studies.

Possibly the increased risk of brain tumors could be the result of laterality recall bias. Yet, as would be expected the ipsilateral ORs are greater than the contralateral ORs in all

3 findings suggesting there was little or no laterality recall bias.

Of the remaining 9 Interphone brain tumor studies, 3 studies had no cases that had used a cellphone for ≥10 years, and 3 of the studies with cases that had used a cellphone for ≥10 years did not report laterality results [7,9,10]. The Lönn et al. study did find non-significant glioma increased risks for ≥10 years since first ipsilateral use and for ≥10 years duration of "regular" ipsilateral use (OR = 1.6, CI: 0.8 to 3.4, $p = 0.19$, based on 15 cases, and OR = 1.8, CI: 0.8 to 3.9, $p = 0.14$, based on 14 cases, respectively), and similar increased meningioma risks were found for ≥10 years of ipsilateral use and ≥10 years duration of "regular" ipsilateral use (OR = 1.3, CI: 0.5 to 3.9, based on 5 cases, and OR = 1.4, CI: 0.4 to 4.4, based on 4 cases, respectively) [8]. Every Interphone Odds Ratio for ≥10 years of ipsilateral cellphone use reported an increased risk (OR > 1.0).

This suggests that when the two highest exposures reported in the Interphone study are combined (≥10 years of use and ipsilateral use), the resultant increased risk offsets the overall systemic protective skew resulting from the Interphone Protocol's flaws, and an increased risk is found in spite of the systemic protective skew. If true, whatever the reported risk, the actual risk (flaws removed) is larger.

5. The independently funded Swedish studies led by Dr. Lennart Hardell

These studies had virtually no industry funding and were entirely within a single-country: Sweden. Table 8 compares both sets of studies. Clearly the Interphone studies have more cases than the Hardell studies. However, the Hardell studies have more cases that used a cellphone for 10 or more years. Almost certainly, the larger number of long-term users is because of the considerably longer diagnosis eligibility range (range of brain tumor diagnosis dates when cases are eligible to participate in a study).

Because selection bias increases as the control refusal rate increases, the substantially smaller control refusal rate in the Swedish studies mitigates against any significant selection bias while the 3.6-fold larger Interphone studies control refusal rates enhances the problem of selection bias.

The Swedish studies, with some exceptions: did not examine risks in regions exposed to the cellphone's radiation plume (flaw 8), excluded cases who had died or were too ill to be interviewed (flaw 9), and did not use subjects' billing records (flaw 10). The Interphone studies had all 11 flaws but did include a portion of the cases that had died or were too ill to be interviewed (flaw 9).

In contrast to the Interphone studies results, which appear to be incredulous (i.e., use of a cellphone protects the user from a brain tumor), the Hardell team results are internally consistent if wireless phones (cellphones and/or cordless phones) use is a risk of brain tumors.

- The higher the cumulative hours of use, the higher the risk [35];
- The higher the radiated power, the higher the risk [44];
- The higher the number of years since first use, the higher the risk [35];
- The higher the exposure (tumor on the same side of the head where the cellphone or cordless phone was held), the higher the risk [25,26], and;
- The younger the user, the higher the risk [29].

6. Role of industry

There has been a long history of industry using "science" to counter findings of risk by industry independent scientists [45]. Over many decades multiple industries have perfected a series of techniques used to diminish or delay effective action that is perceived as harmful to their interests [45].

If we examine, the history of tobacco, ionizing radiation, asbestos, and more recently cellphones, we see there has been an extraordinarily long time between first warnings (followed by many more warnings) and the eventual Public Health acknowledgement that there is a problem (Tobacco: 1856–1964; Ionizing Radiation: 1896–1998; Asbestos: 1911–1996; Cellphones: 1993–?) [46].

6.1. Insufficient funding

Arguably, inadequate funding of research projects is the most common reason why previous studies had been unable to detect what was later seen as an obvious risk. Given insufficient funding, many naïve researchers accept the grant and proceed with the best possible study given the financing provided. Here are two examples.

At the 2005 meeting of the Bioelectromagnetics Society a study was presented of rats exposed to cellphone radiation.

Table 8
Comparison of Interphone studies and Swedish Hardell studies.

Study	Total cases	≥10 years of use cases	Controls	Participation refusal rate		Dx eligibility range years	Industry funding	Identified flaws
				Cases	Controls			
Interphone[a]	4378	172	7229	14.1%[b]	40.7%[b]	2.69[b]	$6.1M+	1 to 11
Hardell	2159	289	2162	11.2%[c]	11.3%	6.00	$0	8, 9, 10

[a] Based on 11 single-country Interphone studies published to date (March 2009).
[b] Weighted-average of 11 single country Interphone studies published to date (March 2009).
[c] Weighted-average of two pooled studies, "benign" and malignant brain tumors.

The study used 13 rats in two groups: 5 for cellphone radiation effects on rat brains, and 8 for cellphone radiation effects on rat skin [47]. As would be expected, with such a small group of animals, no effects were found. When the presenter was asked why she had used so few animals, she said France Telecom had not given her sufficient funding to use more animals.

A second example, is the Interphone study, with more than €3.2 million ($5.1M) of industry money for European research teams [27], and another $1 million from the Canadian Wireless Telecommunications Association (CWTA) [40]. The overwhelming majority of significant Interphone study findings found cellphone use *protects* the user from brain tumors. As discussed above, adequate funding could have eliminated or substantially mitigated the numerous flaws that can account for this incredulous result.

7. Potential public health impact

What is the potential public health impact if cellphone use induces brain tumors? The answer is we do not know, but it is possible to make a rough estimate based on information we have. We can use the CTIA cellphone subscriber data by year [48], and assume that there is a 30-year time delay between first cellphone use and the diagnosis of a brain tumor (latency time). We can also assume that 10% of long-term cellphone users will be diagnosed with a brain tumor, similar to 10% of long-term smokers diagnosed with lung cancer. The result is Fig. 1, which estimates the potential number of cellphone-induced brain tumors by year in the United States. Since Fig. 1 is based on a mathematic model, it can be legitimately challenged (even by this author), and the numerical assumptions adjusted. However, this author finds the shape of the graph, a long time delay followed by a rapid increase in brain tumors, to be highly credible.

As can be seen in Fig. 1, for many years, only a minute number of cellphone-induced brain tumors would be predicted each year (invisible on the scale of the graph). By 2004, the most recent year US brain tumor diagnosis data is available there remains an imperceptible ∼1900 cellphone-induced brain tumors. In 2004 the model calculates there would be about 1900 cellphone-induced brain tumors out of ∼50,000 brain tumors diagnosed that year [49]. By 2009 an increase can be seen in the graph (but the incidence of brain tumors would not be reported by the government until 2013). After 2009 there is a very rapid increase. The model predicts there will be ∼380,000 cellphone-induced brain tumors in 2019.

This would overwhelm the United States public health system. The cost of treating brain tumor patients is on the order of $250,000 per patient [50]. This translates to a $9.5B cost in 2019. Since this would also require roughly a 7-fold increase in neurosurgeons within the next 11 years, surgery for the vast majority of cases would not be an option, so the estimated $9.5B cost would be far less due to lack of treatment resources.

8. Precautionary Principle

Simply put, the Precautionary Principle (PP) is a policy that says if there is some evidence that a problem may exist and low, or no-cost remedial actions are possible, then these actions should be undertaken. Colloquially, we say, "Better safe than sorry." If cellphones induce brain tumors the potential public health costs are large. There is also a simple action that can reduce the absorbed cellphone radiation by several orders of magnitude.

Cellphone radiation decreases as the square of the distance from the phone. As a result even small changes in distance

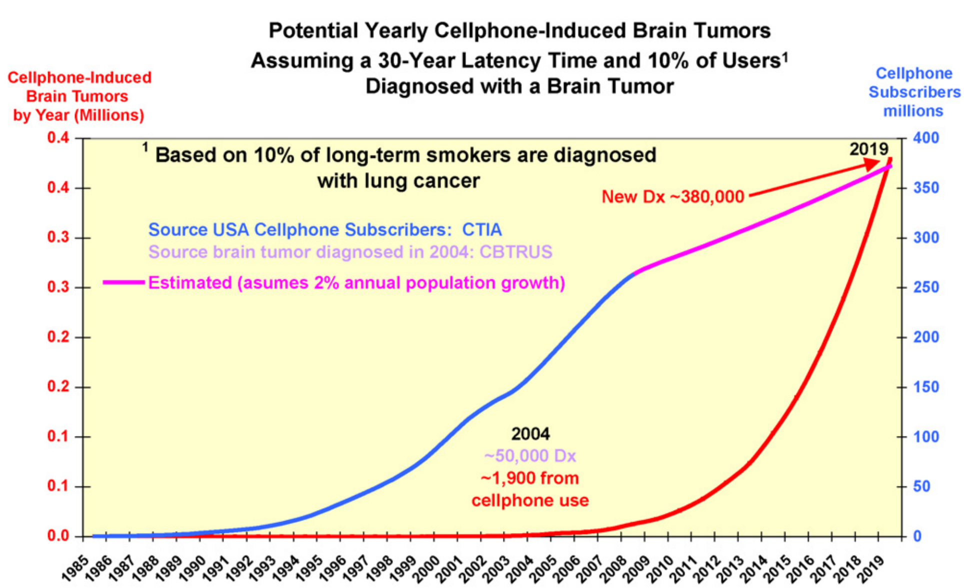

Fig. 1. Long-delay followed by sudden onset of brain tumor epidemic.

have a dramatic effect. For example, when the speaker on the cellphone is placed to the ear, the cellphone is 2 mm from the head and if the cellphone is held 200 mm (100 times) from the head, this change in distance would result in a 10,000-fold reduction in the radiation absorbed by the head.

With use of a headset (not a wireless headset) connected to a cellphone the cellphone is not held directly against the ear and thus the absorbed cellphone radiation could be reduced by several orders of magnitude.

An appropriate PP action would be to mandate cellphone manufacturers to remove the existing cellphone speaker that is placed to the ear and replace it with a headset directly connected to the cellphone. The cost would be near zero (potentially a net cost savings): remove one cellphone speaker—add another speaker (AKA headset).

9. Conclusions

The industry-funded Interphone study has assured the public there is no risk of brain tumors from cellphone use. Yet, a closer analysis of the data leads to the incredulous conclusion that cellphone use protects the user from brain tumors ($p = 6.2 \times 10^{-20}$). A more likely explanation of the data is that the studies were flawed and that there is a link between cellphone use and brain tumors. The Swedish team studies, independent of industry funding, have reported increased brain tumor risk from cellphone use and cordless phone use.

The long history of corporate funded "science" delaying effective action against toxic agents, in some cases up to 100 years, argues convincingly for application of the Precautionary Principle. This is especially true in light of the potentially enormous public health impact should cellphones be shown to cause brain tumors.

The Precautionary Principle clearly applies in this case, since the problem is possible but not certain, and low cost ameliorating actions are easily implemented by industry. With over 3 billion people using cellphones, and with children among the heaviest users, it is time for governments to mandate precautionary measures to protect their citizens.

Conflicts of interest

None.

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