Interphone Brain Tumors Studies To Date

An Examination of Poor Study Design Resulting in an UNDER-ESTIMATION of the Risk of Brain Tumors

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Introduction

As will be seen, the dominant results from all Interphone studies published to date is
use of a cellphone ***protects*** the user from a brain tumor.

There are two possible conclusions from these results:
1) Cellphone use does protect the user from brain tumors, or
2) The Interphone Study is fundamentally flawed.

- All ORs in 10 Interphone brain tumors studies were counted.
- Redundant ORs were removed to obtain a count of statistically independent ORs
- The results show there is a persistent protective skew, statistically so strong as to report it is

virtually certain this protective effect is not due to chance.

Methodology

What If There Is No Risk of Brain Tumors?

(Odds Ratios = ORs)

- Expect: Odds Ratios would be randomly distributed
  - # of ORs <1.0 would be ~equal to # of ORs>1.0
  - Think coin tossing
    - OR=1.0 are excluded
  - OR<1.0 implies protection
  - OR>1.0 implies risk
- 13 Interphone brain tumor studies published to date
  - 10 single-country Interphone brain tumor studies analyzed
    - Excluded: 3 multi-country studies overlapping the single-country studies

Calculation Methodology

- Tally the total number of ORs>1.0, ORs<1.0, and ORs=1.0
- Tally the number of statistically independent (non-redundant) ORs
- Calculate the Protection/Risk ratio (OR<1.0/OR>1.0)
- Calculate the cumulative binomial p-values
  - Think: probability of tossing a coin 20 times and getting 18 heads
  - Answer: $p=2.01 \times 10^{-4}$, or 1 time in 4,970 it will be due to chance.

Methodology
Requires Statistical Independence

- Comparison categories
  - Brain Tumors
    - All
    - Acoustic Neuroma
    - Glioma
    - Meningioma
  - Years since first use (Years)
  - Cumulative hours of use (Hours)
  - Cumulative number of calls (Call #)
  - “Regular” cellphone use (“Regular”)
  - Years of ipsilateral cellphone use (Years Ipsi)
  - Years of contralateral cellphone use (Yrs Contra)
  - Minutes of cellphone use per day (Min/Day)
- Category comparisons between studies, not within studies

Results

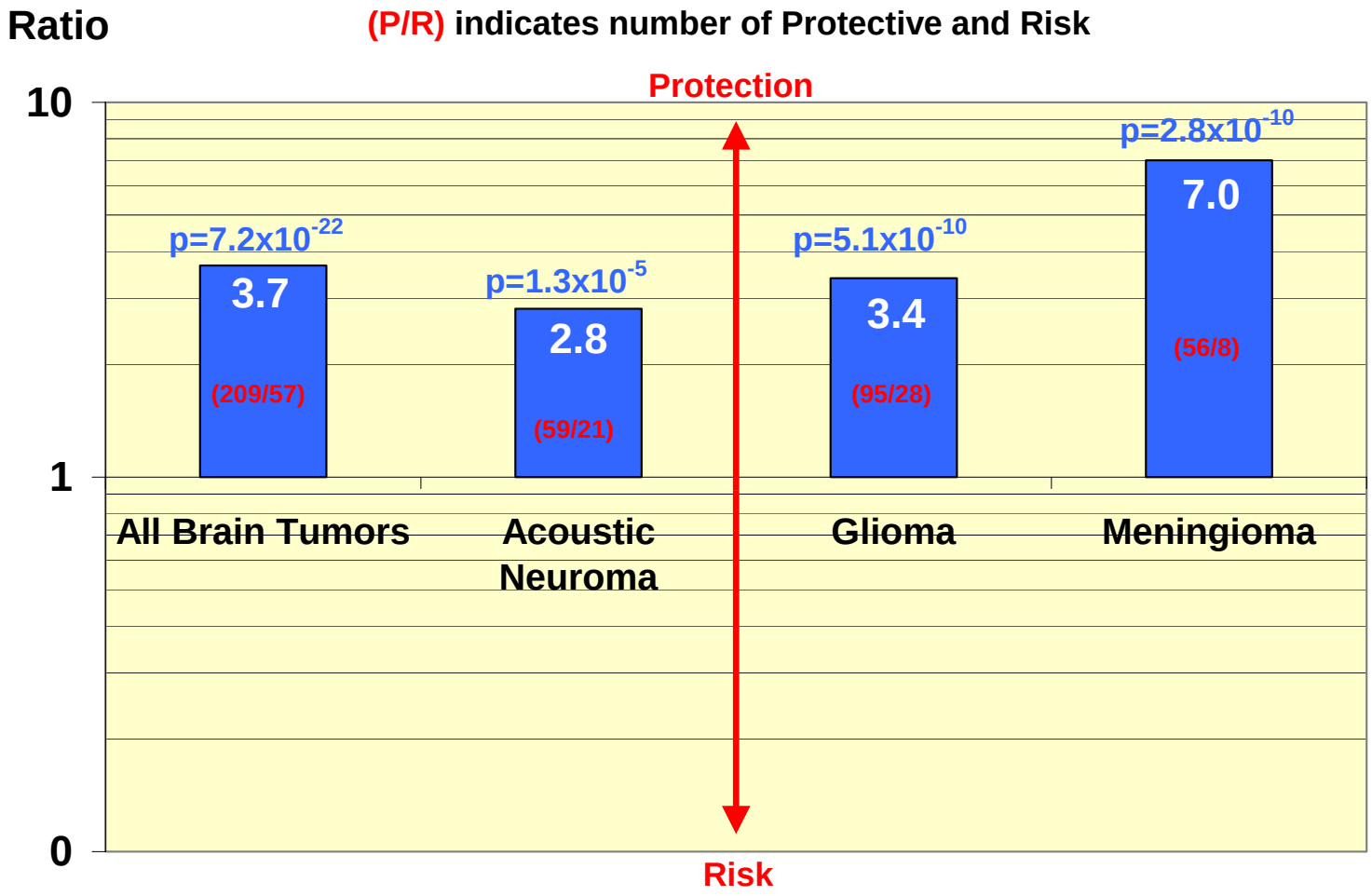
Total ORs and Statistically Independent ORs
(OR=1.0 Excluded)

	Total	Independent	% Ind.
Acoustic Neuroma	160	96	60%
Glioma	234	125	53%
Meningioma	124	64	52%
All Brain Tumors	518	285	55%

OR=1.0 are 1.5% of all Odds Ratios

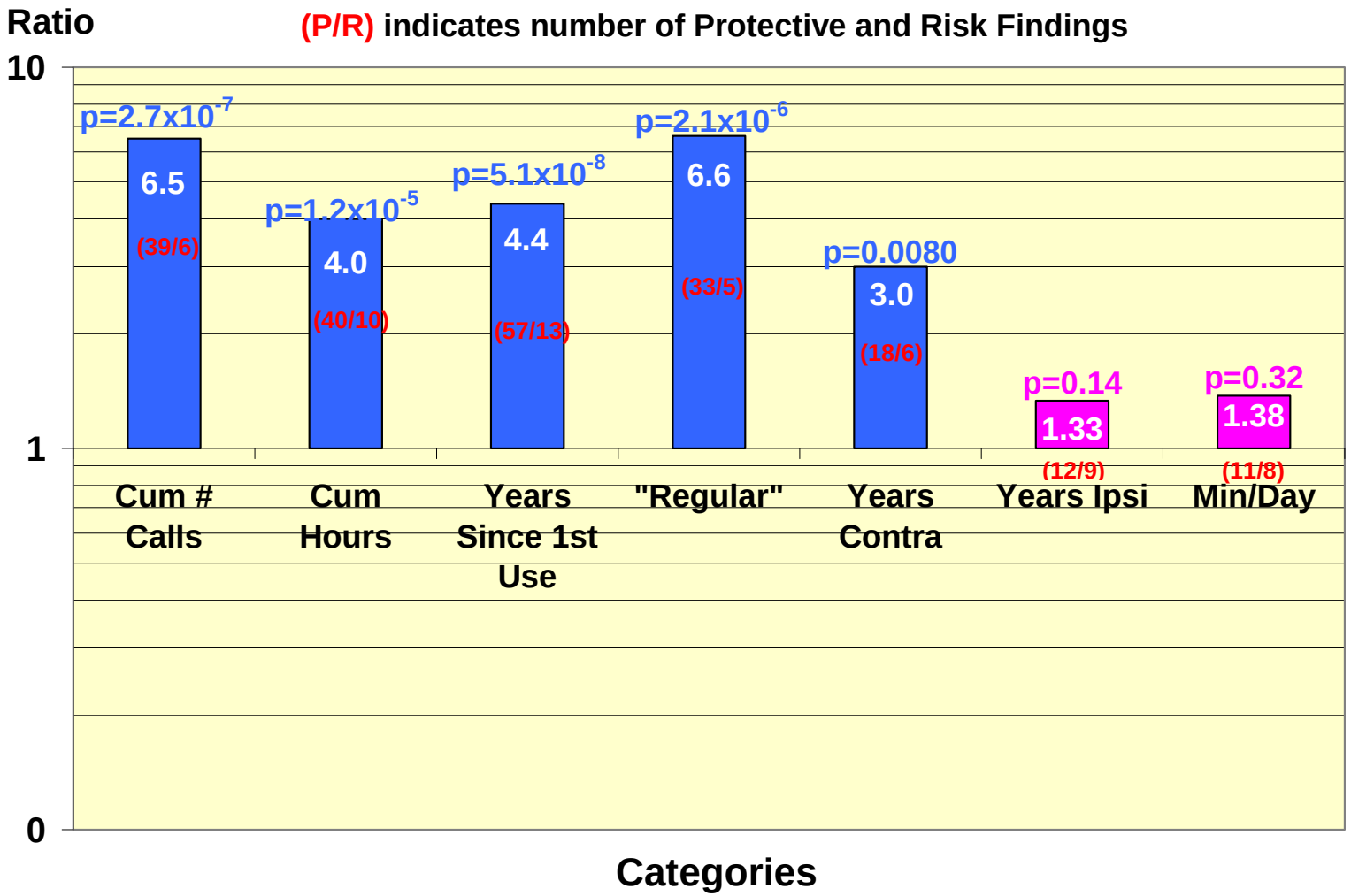
Results

Protection/Risk Ratio by Brain Tumor Type



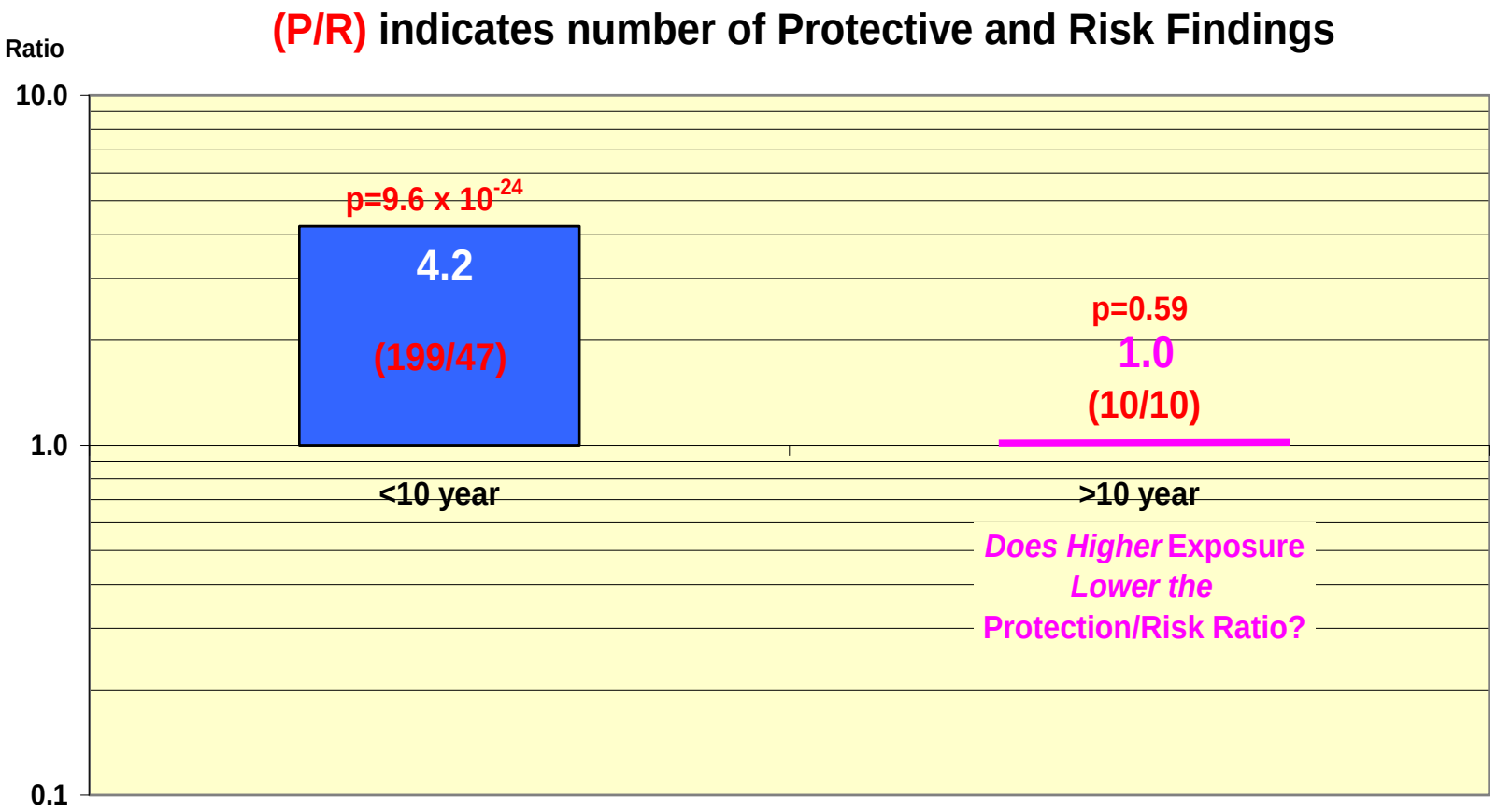
Results

Protection/Risk Ratio by Category



Results

Lower Vs Higher Exposure Time



Interphone Protocol Design Flaws

- Flaw 1: Selection Bias
  - Reasonable to assume that controls who use a cellphone are more likely to participate in a "cellphone study" than controls who do not use a cellphone
    - Selection bias increases as the refusal rate increases
    - Weighted average control refusal rate: 41%
      - Is there selection bias? (Löon 2004)
        - » 34% of controls who refused to participate used a cellphone
        - » 59% of participating controls used a cellphone
  - Underestimates risk

Flaw 1: Selection Bias

A Semi-Hypothetical Example

With Selection Bias

	Exposed	Unexposed	Totals
Cases	60	40	100
Controls	60	40	100
Totals	120	80	200
Odds Ratio	1.00		

Without Selection Bias

	Exposed	Unexposed	Totals
Cases	60	40	100
Controls	49	51	100
Totals	109	91	200
Odds Ratio	1.54		

Truly Exposed Controls=(60 "exposed" controls) * (59% participants) + (34 non-participanting controls) * (40% non-participants)=49

Interphone Protocol Design Flaws

- Flaw 2: Exposure Misclassification
  - Tumors outside the radiation plume are treated as "exposed"
    - Overestimates risk of brain tumor
  - **Ipsilateral: exposed Contralateral: unexposed**
  - Percentage of absorbed cellphone radiation by anatomical structure in adults
    - Ipsilateral temporal lobe: 50-60% ~15% of brain's volume
    - "Ipsilateral" cerebellum: 12-25% ~5% of brain's volume
    - **62-85% of absorbed radiation is in ~20% of the adult's brain volume**
    - *Children's brains will absorb a higher values***.**

Flaw 2

A Semi-Hypothetical Example

With Flaw 2 Design Error

	"Exposed"	Unexposed	Totals
Cases	75	25	100
Controls	60	40	100
Totals	135	65	200
Odds Ratio	2.0		

Without Flaw 2 Design Error

	Exposed	Unexposed	Totals
Cases	15	85	100
Controls	12	88	100
Totals	27	173	200
Odds Ratio	1.3		

Truly exposed cases=(75 "exposed cases")*(20% truly exposed)=15. Truly exposed controls=(60 "exposed controls)*(20% truly exposed)=12

Interphone Protocol Design Flaws

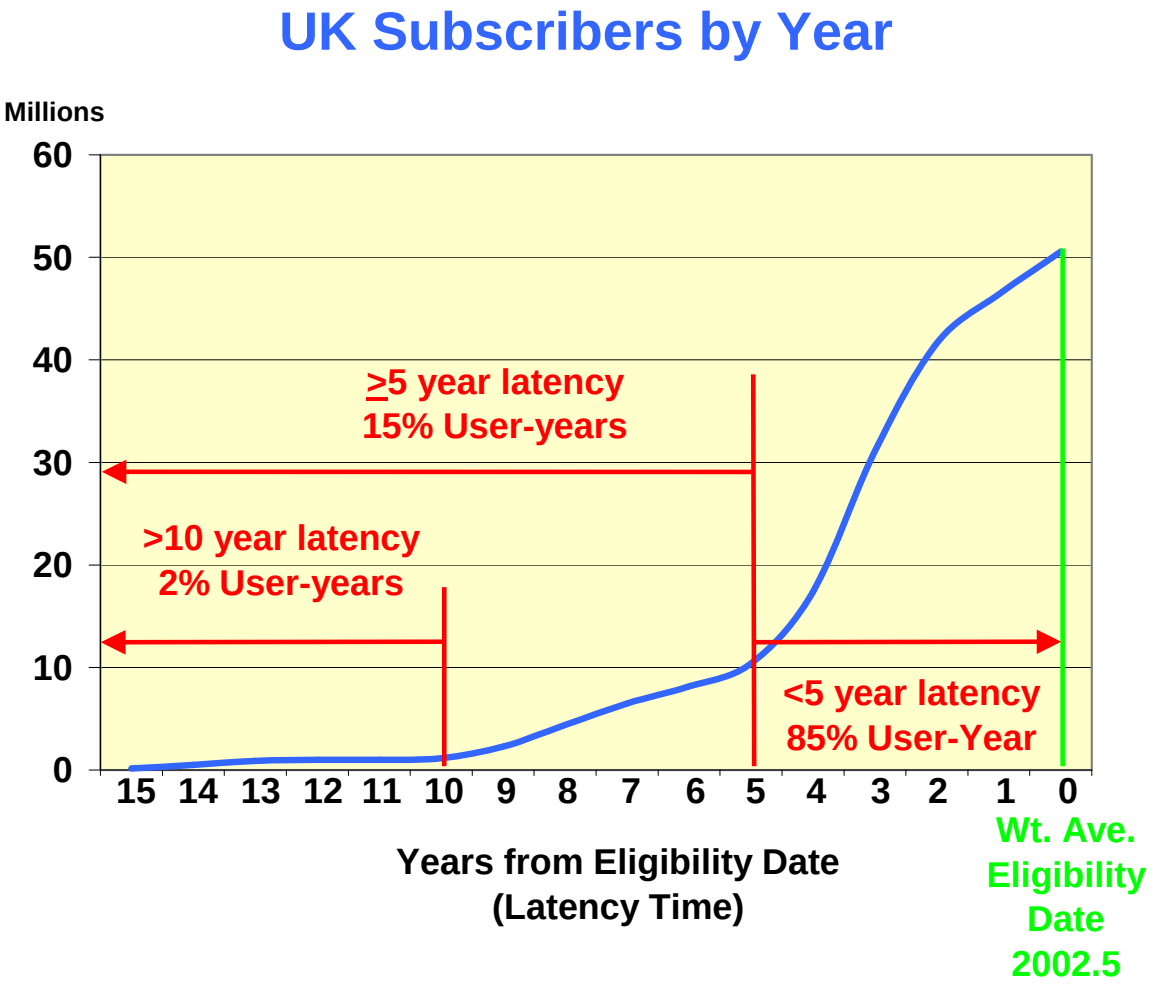
- **Flaw 3:** Short latency times
  - Known latency times
    - Smoking & lung cancer: ~30 years
    - Asbestos & mesothelioma: 20-40 years
    - Ionizing radiation & brain tumor: 20-40 years
  - Only 6.3% of Interphone cases (16 cases/study) used a cellphone for ≥10 years
  - Short latency times underestimates risk
- Flaw 4: Definition of "regular" user
  - At least once a week for 6 months or more
    - Exposures one prior to diagnosis are excluded
  - Definition of "regular" user underestimates risk

Flaws 3 & 4: Latency Time & "Regular" Use

- UK cellphone subscriber data
  - 85% of "regular" use
    - <5 years
  - 98% of "regular" use
    - <10 years
- Reporting "regular" use
  - Suppresses finding a risk
- Expect 20 to 40 years for brain tumor Dx
  - Years of cellphone use (latency) is too short for Dx

Flaws 3 and 4

Latency Time and the Definition of "Regular Users"



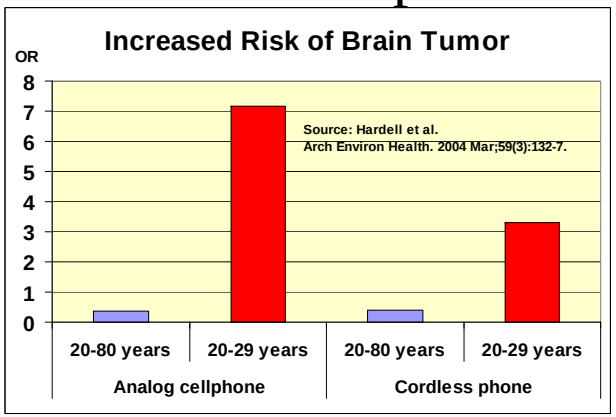
Interphone Protocol Design Flaws

- Flaw 5: Young adults and children are excluded
  - Interphone Protocol's age range: 30-59
    - Young adults and children are the highest risk group
  - Underestimates risk

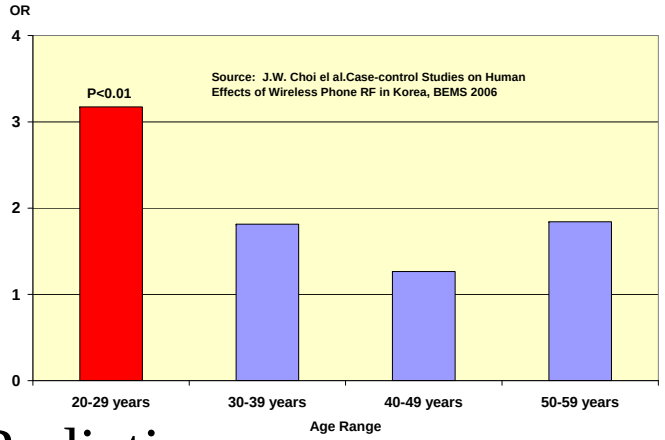
Flaw 5

Young Adults and Children Excluded

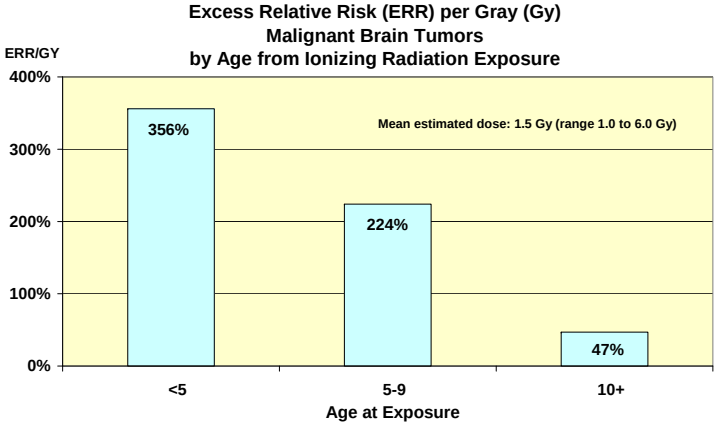
Swedish: Cellphone.



Korean: Cellphone



Israeli: Ionizing Radiation



Source: Sadetzki et al., RADIATION RESEARCH 163, 424–432 (2005)

Interphone Protocol Design Flaws

- Flaw 6: Cellphones radiating higher power levels are not examined (few exceptions)
  - Analog Vs Digital cellphone use
  - Rural Vs Urban digital cellphone use
  - Without inclusion of cellphones radiating the most power there is an underestimation of risk
    - Requires sufficient number of cases for statistical power
- Flaw 7: Cordless phone users are treated as unexposed
  - Underestimation of risk

Flaw 7: Semi-Hypothetical Example

Assumptions:

36% of Swedish cellphone users do not use a cellphone or cordless phone

57% of Swedish do not use a cellphone

There is a 2-fold risk of brain tumors from cellphone use or cordless phone use

Cordless Phone Exposure Treated As Un-Exposed

	Exposed	Unexposed	Totals
Cases	43	57	100
Controls	27	73	100
Totals	70	130	200
Odds Ratio	2.0		

Cordless Phone Exposure Treated As Exposed

	Exposed	Unexposed	Totals
Cases	64	36	100
Controls	40	60	100
Totals	104	96	200
Odds Ratio	2.6		

Interphone Protocol Design Flaws

- Flaw 8: Exclusion of brain tumor types
  - Includes acoustic neuroma, glioma & meningioma
  - Excludes other brain tumor types
  - Underestimates risk
- Flaw 9: Exclusion of brain tumor cases because of death
  - Underestimates risk of the most deadly brain tumors

Interphone Protocol Design Flaws

- Flaw 10: Recall bias
  - Light users tend to underestimate use
  - Heavy users tend to overestimate use
  - Result: Underestimation of risk

Flaw Mitigation

- Increase the diagnosis eligibility time
  - Ten Interphone studies: weighted-average 2.6 years
  - Hardell et al. studies: 6 years
- Lower minimum age from 30 years to 10 years
- Do not tell controls what is the purpose of the study
  - Pay cases and controls for participation in study
- Interview proxies in case of death
- Treat unexposed tumors as unexposed
- And, so on, and so on, and so on …
  - **It could have been done**

Conflicts-of-Interest

- 2008 Global Telecom Industry Revenue: $3.85 Trillion (£6.8T)
  http://www.plunkettresearch.com/Telecommunications/TelecommunicationsStatistics/tabid/96/Default.aspx
  - If risk is admitted: major revenue loss
  - Interphone's funding is inadequate to mitigate flaws
    - Substantial funding from cellphone industry
      - €3.2 million (£4M) in Europe, $1M (£0.6M) in Canada, unknown in Japan, Australia and New Zealand
- Government
  - UK
    - £22.5 billion (~$40B) selling off the 3G licences
    - Annual income of around £15 billion (~$27B) in taxation to the UK exchequer
  - Similar industry funding goes to all governments

Conflicts-of-Interest

- Researchers' conflict-of-interest
  - Perhaps unconscious, but they know industry has funded their studies in spite of a "Firewall"
  - Firewall: Industry send funds to 3rd party group
    - 3rd party selects and funds research teams
  - Honest, but "Don't bite the hand that feeds you"
    - **33 *significant protective* results**
      - **Ignored by authors (no commentary in the text)**

Conclusions

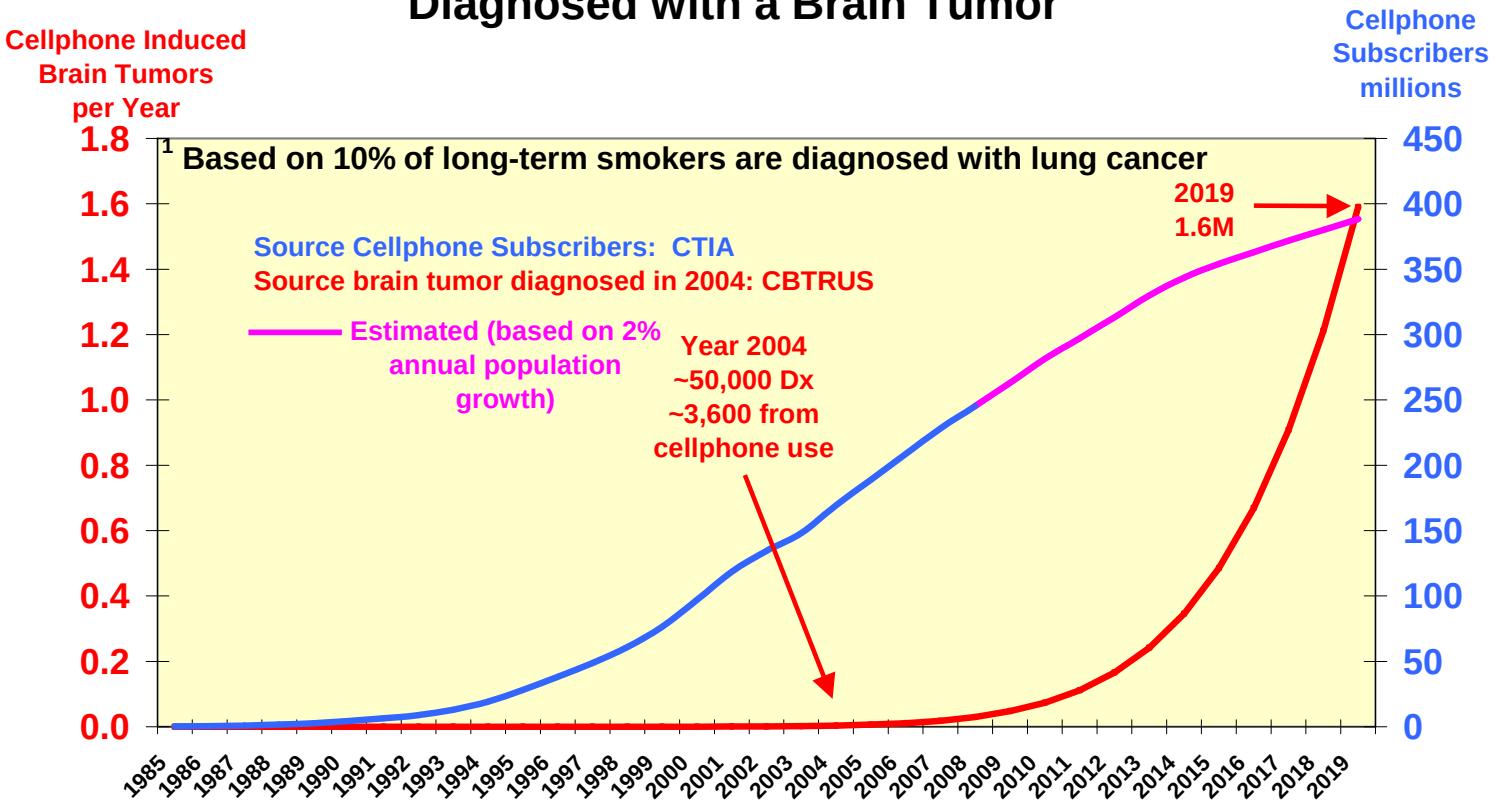
- **There is certainty: either cellphone use is protective, or the Study has major flaws**
- The Interphone Protocol *substantially*, underestimates the risk of brain tumors
  - In spite of the protective skew, significant increased risk is found in the Interphone studies
    - When ≥10 years ***and*** ipsilateral use are combined
      - Increased exposure counteracts design flaws' protective skew?
- Without design flaws, risk would increase substantially
- Cellphone industry's conflict-of-interest is obvious
- **Potential public health impact is enormous**
- Studies independent of industry are required

Cellphone Studies Independent of Industry Funding

- Swedish team led by Dr. Lennart Hardell
  - Findings consistent with what would be expected, if there is a risk of brain tumors from wireless phone use
    - The higher the cumulative hours of use, the higher the risk
    - The higher the radiated power, the higher the risk
      - Analog Vs Digital cellphones
      - Rural Vs Urban users
    - The higher the number of years since first use, the higher the risk
    - The higher the cumulative number of calls, the higher the risk
    - The higher the exposure, the higher the risk
      - Tumor on the same side of the head where the cellphone was used
    - The younger the user, the higher the risk

Potential Public Health Risk

Potential Brain Tumor Cases From Use of a Cellphone
Assuming a 30-Year Latency Time and 10% of Users[1] Diagnosed with a Brain Tumor



I Pray I'm Wrong!

Potential Brain Tumor Risk
30-year Latency

Poisson Distribution Calculation