

Should we Hang Up on the Debate about Cell Phones and Cancer Risk?



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Overview

- Cell phones (mobile phones) and cancer risks:
 - > rationale for studies
 - > characteristics of exposure
 - > biological effects
 - > results of epidemiologic studies
 - > strategies for reducing exposure
- Other radiofrequency radiation exposures & cancer risks
- Methodologic & other challenges in studying cancer risks associated with cell phone use
- Scientific gaps
- Ongoing research

Cell Phones & Cancer: Public Concerns

CLOSE UP

How risky is cell-phone radiation?

The Food and Drug Administration says the “weight of scientific evidence has not linked cell phones with any health problems,” including brain tumors from the low-level radiation that phones emit in normal use. Yet in the past year San Francisco lawmakers have enacted an ordinance requiring that cell phones disclose the amount of radiation emitted, and Rep. Dennis Kucinich (D-Ohio) announced plans to push for radiation warnings on all cell phones.

Phone manufacturers are required by federal law to package every cell phone with information about its specific

values only to ensure that maximum radiation exposure falls below the level at which experts agree there could be adverse health effects.

Still, consumers are caught in the middle, trying to resolve conflicting messages from regulators and legislators. (The latter include those in the European Parliament who have called for stricter limits on exposure to cell-phone radiation, which have been criticized by many scientists.)

Consumers Union believes a number of measures would benefit consumers:

- The U.S. needs a national research

The **TRUTH** About Cell Phone **RADIATION**,
What the **INDUSTRY** Has Done to Hide It, and
How to **PROTECT** Your **FAMILY**



Disconnect

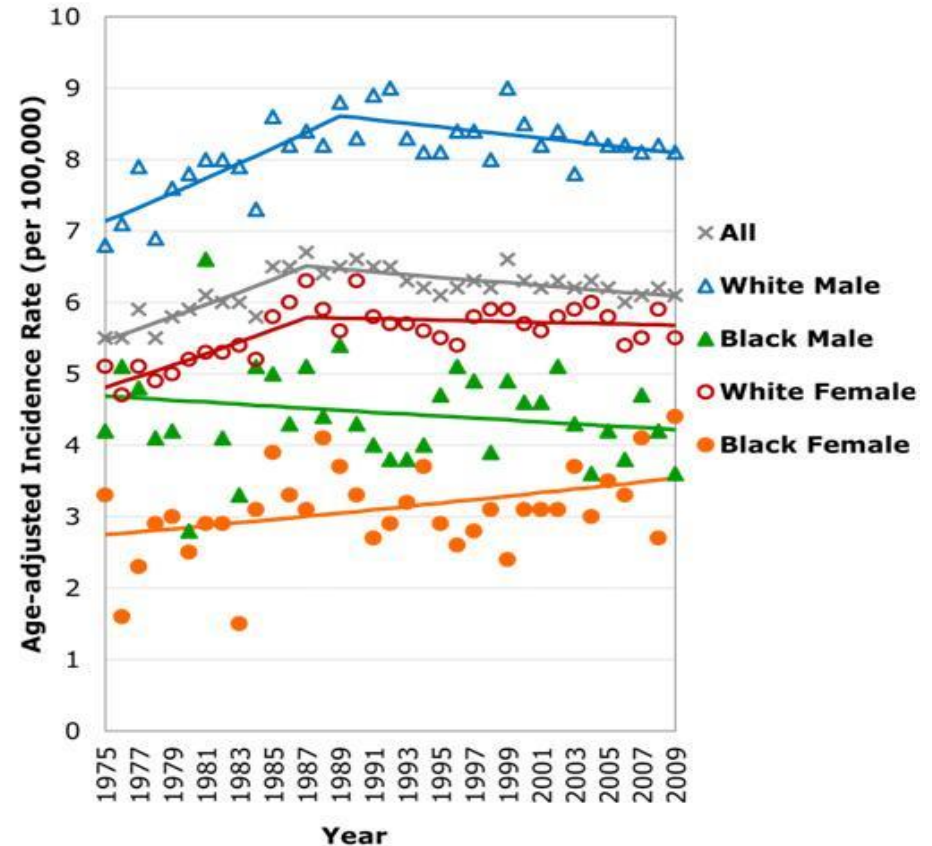
NATIONAL BOOK AWARD FINALIST

DEVRA DAVIS

Foreword by David Servan-Schreiber, author of *Anticancer*

Cell Phones & Brain Tumors: Rationale

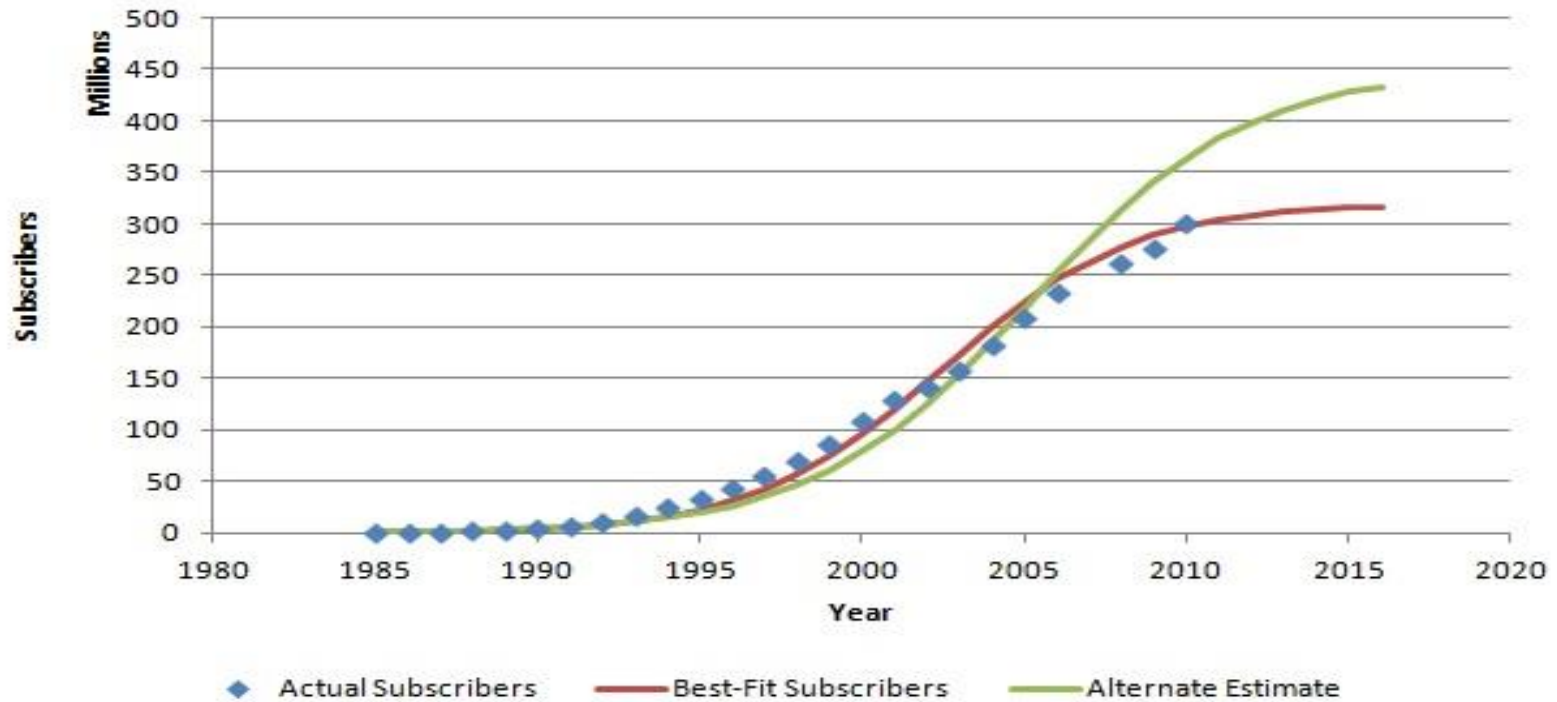
- Radiation & cancer: long-standing concern
- Electromagnetic fields and cancer: passionate & polarized views
- Rapid increase in cell phone use since 1990s
- Rising adult brain tumor incidence 1975-1991 → cell phone & brain tumor studies launched 1994



U.S. brain cancer incidence trends
(SEER Program, 2012)

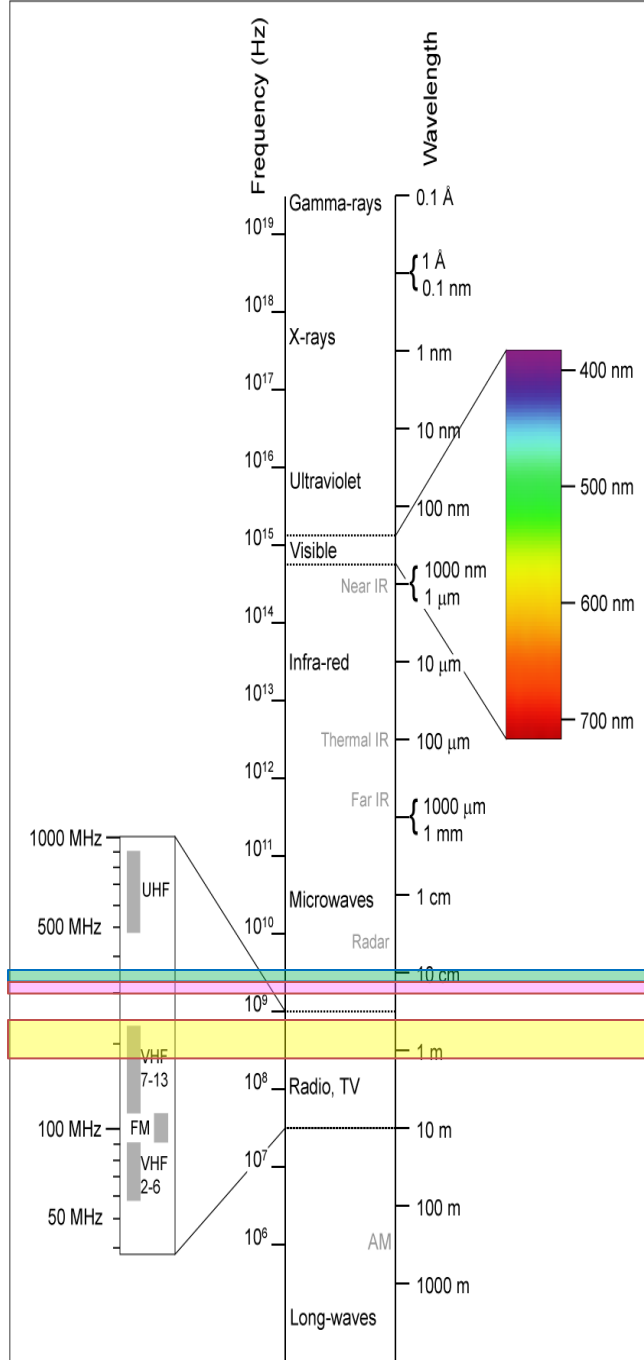
Cell Phone Subscribers in U.S. (1985-2010)*

Annual Cell Phone Subscribers in the United States



*Cellular Telephone Industry Association (CTIA)

Electromagnetic Spectrum



Universal mobile telecommunications system (1900-2200 Mhz)

Digital phones (1800-1900 MHz)

Early analog phones (450 & 900 Mhz)

Population Radiofrequency Exposures

- Exposures ubiquitous, but limited measurements
- Exposures decline notably with increased distance
- Residential sources & levels:
 - cell phones: ≤ 0.25 watt
 - Wi-Fi, microwave ovens and others: indoor levels 1-100 times lower than outdoor levels
- Outdoor exposures to general population:
 - radio & TV transmitters: up to 1 megawatt
 - cell phone base stations: ≥ 1 watt
- Occupational maximum permissible exposure limits:
 - vary with frequency range
 - measured in mW/cm^2 time-averaged

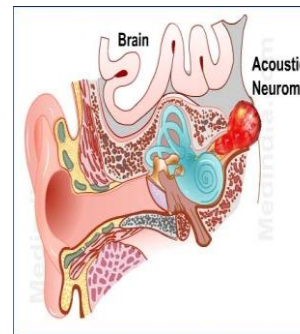
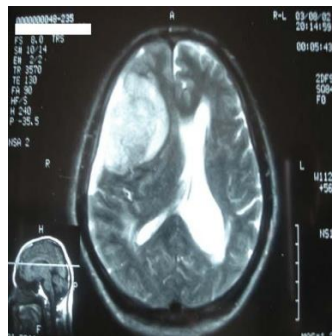
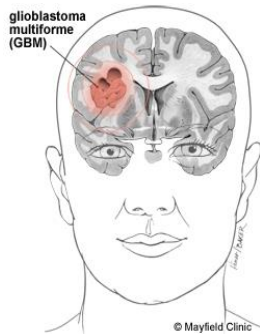
Biological Effects of Radiofrequency Radiation

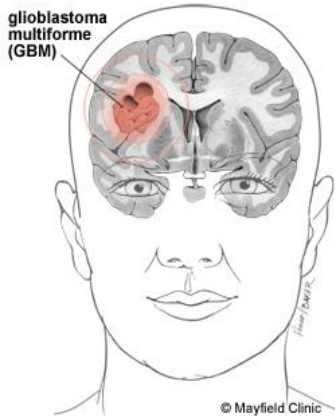
- Radiofrequency radiation energy:
 - insufficient for breaking molecular bonds
 - most exposures are orders of magnitude less energy than x-rays
- Primary biological effects:
 - thermal
 - > measureable at high power levels
 - > minimal at low power levels (cell phones)
 - non-thermal
 - > activation of proteins and genes; unclear relevance to long-term effects
- Conundrum for animal studies:
 - exposures need to be higher than typical exposures experienced by humans
 - need to avoid thermal effects



Early Epidemiological Studies

- 1993: anecdotal TV report
 - Congressional hearings
 - trade industry (CTIA) commits \$25 million
- 1994: 4 studies launched
 - 3 case-control studies
 - 1 cohort study Denmark





Summary: Early Studies of Gliomas

- Exposure assessment:
 - case-control studies: questionnaires
 - cohort study: subscriber listings
- Case-control studies: No associations
- Cohort study: No excess in subscribers vs non-subscribers

Unresolved Issues following Initial Studies

- No information on long-duration, heavy users
- Relevant surrogate exposure metric unknown:
 - years of regular use?
 - cumulative numbers of phone calls?
 - cumulative hours of use?
 - other?
- Biological and mechanistic issues in carcinogenesis

Next Generation of Epidemiologic Studies

- Extended follow-up of Danish Cohort Study (2006; 2011)
- INTERPHONE case-control studies (13 countries pooled data)
 - individual study publications (2002-2008)
 - pooled study (2010)

Extended Danish Cohort Study*

- 358,403 persons with first cell phone subscriptions in 1987-1995 and followed up through 2007
- Compared incidence >10 yrs use vs. non-subscribers

CNS tumor type	Sex	IRR	(95%CI)
Glioma	Men	1.04	(0.85 – 1.26)
	Women	1.04	(0.56 – 1.95)
Meningioma	Men	0.90	(0.57 – 1.43)
	Women	0.93	(0.46 – 1.87)

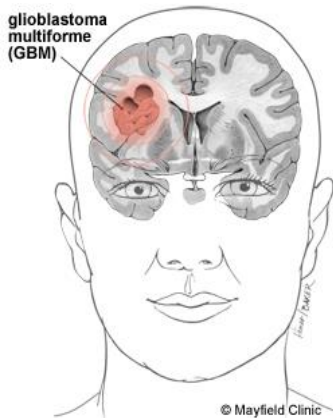
- No increase in risk among subscribers with >10 years use

*Frei et al. *BMJ*, 2011

INTERPHONE* Study of Brain & Other Tumors*

- Denmark
- Finland
- Norway
- Sweden
- United Kingdom
- Germany
- France
- Italy
- Israel
- New Zealand
- Australia
- Japan
- Canada

*13 countries where cell phones used earlier than in U.S.



Glioma – INTERPHONE Study

- 2,708 glioma patients (64% participation); 2,972 controls (53% participation)
- Reduced risks for years since 1st use, duration of use, cumulative number of calls, and for digital phone use
- ↑ risks for highest decile of call time: OR = 1.40, 95%CI = 1.03-1.89)
- ↑ risk for use on same side of head as tumor, but ↓ risk on opposite side of head, BUT risks highest for short-term users

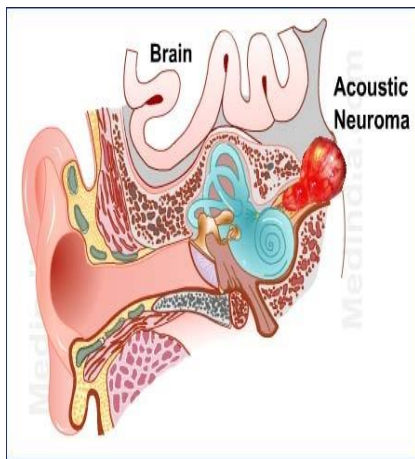
*INTERPHONE Study Group. *Int J Epidemiol* (2010)

Meningioma – INTERPHONE Study



- ORs < 1.0 in lowest 9 deciles of cumulative call time, and OR=1.15, 95%CI=0.81-1.62) in highest decile
 - > No excess risk among medium and long-term users, but ↑ risk in short-term users
- Reduced risks for temporal lobe tumors for regular use and for all metrics; same for other anatomic sites
- Borderline elevated risk for tumors on same side as phone use (OR=1.07, 95%CI=1.00-1.16)

*INTERPHONE Study Group. *Int J Epidemiol* (2010)



Acoustic Neuroma – INTERPHONE Study*

- 1,105 cases, 2,145 controls
- Risk estimate: [OR (regular use = 0.85; (CI:0.69-1.04)]
- No overall increase in risk for cumulative hours of use, duration of use
- Non-significant increase in 10th decile of cumulative use, but notable ↓↓ in 9th decile
- No excess for use of phone on same side of head as tumor

*INTERPHONE Study Group. *Cancer Epidemiol* (2011)

Summary of INTERPHONE Results- 1

- Conclusions for glioma and meningioma:
 - > “overall no increase...”
 - > “for glioma...suggested increases at highest exposure levels, but biases and errors prevent causal interpretation”
 - > “for meningioma...little evidence to counter a global null hypothesis”
 - > “the possible effects of long-term heavy use of mobile phones require further investigation”

Summary of INTERPHONE Results - 2

- Conclusions for acoustic neuroma:
 - > no overall association
 - > non-significant increase in 10th decile of cumulative use could be due to chance

Case-Control Studies of Cell Phone Use and Malignant Brain Tumor Risk in Sweden*

- Population:
 - > incident cases adults ages 20-80
 - > 1,251 cases (85% participation) vs. 2,438 matched (age, sex, region, & vital status) population controls (84% participation)
- Exposure assessment:
 - > self-administered questionnaires to subjects or next of kin
- Results:
 - > ↑ risk with increasing latency & cumulative hours of use
 - > highest risks for glioma with >10 yrs latency (OR=2.7, 1.9-3.7) and with first use before age 20 *OR=4.9, 2.2-11)


International Agency for Research on Cancer


- IARC: Vol 102, 2013
- Classified cell phone use/RF exposure 2B
- Basis of assessment:
 - > INTERPHONE results
 - > Swedish pooled case-control studies

IARC Monograph on RF

• **Volume 102: Non-ionizing Radiation, Part 2: Radiofrequency Electromagnetic Fields, 2013**

- Expert meeting, May 2011
- *The Lancet Oncology*, 22 June 2011
- Monograph publication, 24 April 2013



30 | ITU Workshop on EMF | Turin | 9 May 2013  World Health Organization

IARC CLASSIFICATION Other Agents	
Class	Agent
Group 1 (Carcinogenic)	Asbestos Ionizing Radiation Tobacco
Group 2-A (Probable, >50% risk)	Acrylamide Styrene UV Radiation
Group 2-B (Possible, <50% risk)	Chloroform Coffee ELF/ RF
Group 3 Lack of Evidence	Polystyrene Tea Surgical Implants
Group 4 Not Carcinogen	Caprolactam (Precursor to Nylon)

Epidemiologic Studies Post IARC Report

Cohort design: Million women prospective study*

- 791,710 women followed up an average of 7 years
- 571 gliomas, 251 meningiomas, 96 acoustic neuromas
- gliomas & meningiomas: no associations for ever or for 10+ years use
- acoustic neuroma: increased risk for long-term use & dose-response trend

* Benson VS et al. *Int J Epidemiol* (2013)

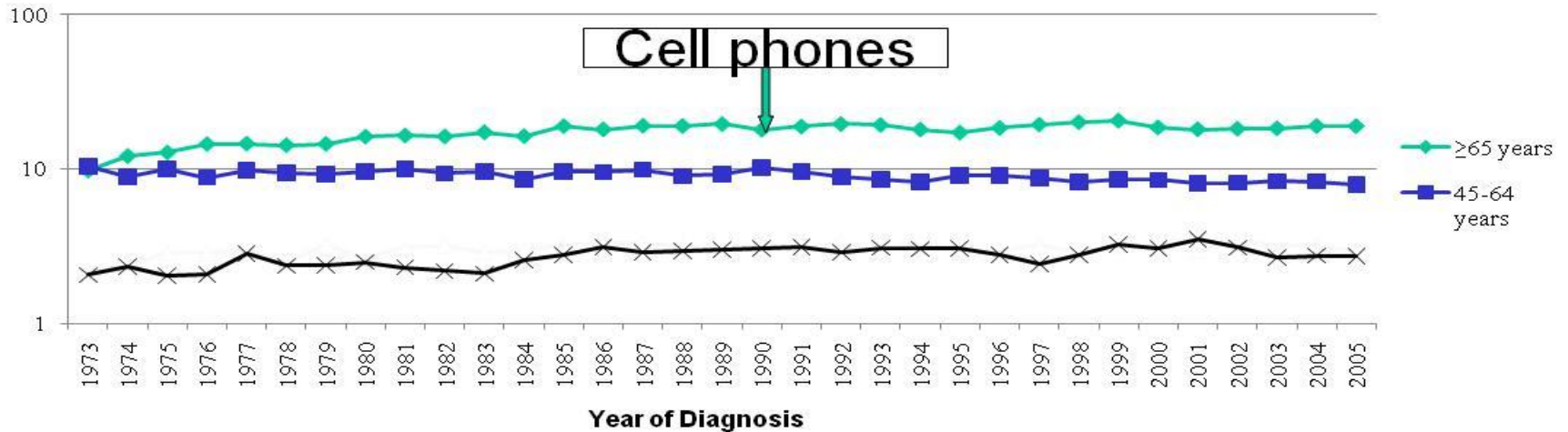
Case-control design: CERENAT§

- 253 gliomas, 194 meningiomas, 892 controls
- participation: gliomas (66%), meningiomas (75%), controls (45%)
- ↑ gliomas & meningiomas with cumulative hours of use
- ↑ gliomas with occupational use, urban use
- ↑ gliomas on same side as use but ↓ ↓ on opposite side

§ Coureau G et al. *Occup Environ Med* (2014)

Incidence trends in CNS tumors

Trends in Brain Cancer Incidence By Age, 1973-2005 (SEER)



- Inskip PI et al (2010); Glioma incidence downward or flat in U.S., 1992+
- Deltour I et al (2009): Glioma and meningioma incidence unchanged in Nordic countries, 1998-2003
- Nelson PD et al (2006): Acoustic neuroma incidence \uparrow 3-fold 1980-97 then \downarrow 30% by 2000 in U.S.: most likely reporting & diagnosis

Projected* vs. Observed Glioma Incidence Rates

- Simulated vs observed Nordic glioma incidence rates[†]
 - > Assumed risk of 1.2 – 2.0 and latencies of 5 – 15 years
 - > Excess risks were incompatible with observed 1979-2008 rates
- Projected vs. observed U.S. glioma incidence rates[§]
 - > Projected from Interphone consistent with observed 1997-2008
 - > Projected from Swedish studies at least 40% higher than observed and thus Swedish risks not reflected in U.S. incidence trends

* INTERPHONE Study (2010) and Swedish studies by Hardell L et al (2011)

[†]Deltour I et al. *Epidemiol* (2012); [§]Little MP et al. *BMJ* (2012)

Reducing RF Exposures from Cell Phones*

- Cell phones for short, landlines for longer calls
- Hands-free devices except Bluetooth, which has higher exposures
- Use cell phones with lowest SARs
- Text rather than call (neither when driving)
- Phone on belt or bag



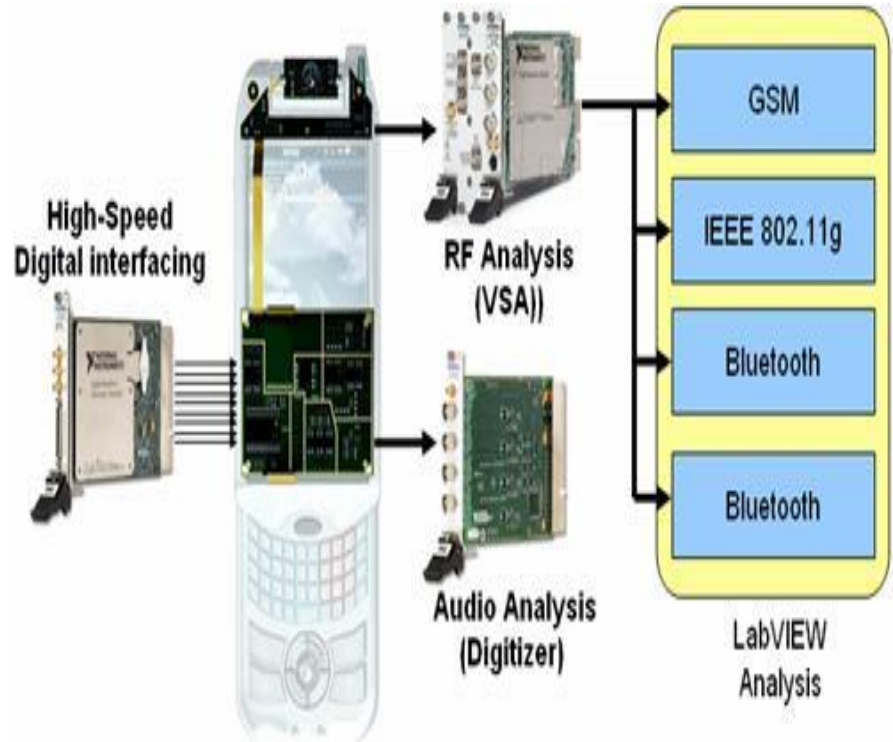
Consumer Reports: 2011, 2015

*U.S. Food and Drug Administration www.fda.gov/Radiation-EmittingProducts/RadiationEmittingProductsandProcedures/HomeBusinessandEntertainment/CellPhones/default.htm
U.S. Federal Communications Commission www.fcc.gov/cgb/cellular.html

Occupational and Environmental Studies of RF Exposure and Cancer Risks

Workers Manufacturing Cell Phones*

- 195,775 Motorola workers 1976-96 followed thru 1996
- RF exposure: job exposure matrix
- No association between RF & brain cancer mortality



*Morgan RW et al. *Epidemiology*, 2000

U.S. Navy Veterans of Korean War*

- 49,581 Navy veterans
- Potential exposure to high-intensity radar
- No ↑ brain cancer
- Increased non-lymphocytic leukemia in subgroup



*Groves FD et al. *Am J Epidemiol*, 2002

Cell Phone Base Stations and Cancer Risk

- Major concern is pediatric cancer risk residing near base stations
- Few studies
- No increase in risk associated with individual level exposures*
- Need better exposure assessment in populations with high RF



*Ha M et al. *Am J Epidemiol* (2007); Merzenich H et al. *Am J Epidemiol* (2008); Elliott P et al. *BMJ* (2009).

Methodological Issues: Focus on INTERPHONE Study

Methodologic Limitations & Associated Investigations - 1

Limitations

- Exposure assessment

Methodologic Investigations

Vrijheid M et al. Determinants of mobile phone output power in a multinational study: implications for exposure assessment. *Occup Environ Med* 2009;66:664-71.

Schüz J & Johansen C. A comparison of self-reported cellular telephone use with subscriber data: agreement between the two methods and implications for risk estimation. *Bioelectromagnetics* 2007;28:130-6.

Cardis E et al. Distribution of RF energy emitted by mobile phones in anatomical structures of the brain. *Phys Med Biol* 2008;53:2771-83.

Methodologic Limitations & Associated Investigations - 2

Limitations

- Selection bias
- Recall errors
- Recall bias

Methodologic Investigations

Vrijheid M et al. Quantifying the impact of selection bias caused by non-participation in a case-control study of mobile phone use. *Ann Epidemiol* 2009;19:33-41.

Vrijheid M et al. The effect of recall errors and of selection bias in epidemiologic studies of mobile phone use and cancer risk. *J Exp Sci Environ Epidemiol* 2006;16:371-84.

Vrijheid M et al. Validation of short-term recall of mobile phone use for the Interphone Study. *Occup Environ Med* 2006;63:237-43.

Vrijheid M et al. Recall bias in the assessment of exposure to mobile phones. *J Exp Sci Environ Epidemiol* 2009;19:369-81.

How Methods Studies Informed Study Results

- INTERPHONE study interpretation:
 - > “We have no certain explanation for the overall reduced risk of brain cancer among mobile phone users...”
 - > “Selection bias is almost certainly a contributor”
 - > “Some evidence that very high users had excess glioma, but inconclusive due to possible bias.”
 - > “Results are uninformative for longer lag periods since few subjects used cell phones more than 12 years.”
- Non-participation bias (non-participants had lower prevalence of cell phone use) could have caused reduction of OR of 5-15%

Challenges in Studying Cell Phone Use and Cancer risks

Challenges in Assessing Cancer Risks Associated with Technological Changes



Challenges in Assessing Cancer Risks Associated with Technological Changes



Mechanisms and Biology Poorly Understood

Limitations

- Relevant metric unknown
- Biologically relevant surrogate measure?
 - cumulative hours of use?
 - duration of use in years?
 - cumulative numbers of calls?
- Mechanism for occurrence of neoplasms unknown
- Tumor biology poorly understood

National Toxicology Program

- large rodent RF studies
- mimic human exposure (up to 10 hrs/day)
- study 900 and 1900 MHz & 2 modulations in U.S
- specially designed labs
- final results in 2016

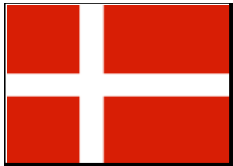
Ongoing Epidemiologic Studies

Rationale for Ongoing Studies

- Research driven by public concern about new communication technologies which have dramatically increased in a short time period
 - To date no clear risks observed but research needed to monitor risks of long term use and/or new applications
 - Prospective studies among adults
 - Childhood studies
-

The Cosmos Project

International Cohort Study of Mobile Phone Use and Health



Denmark



Sweden



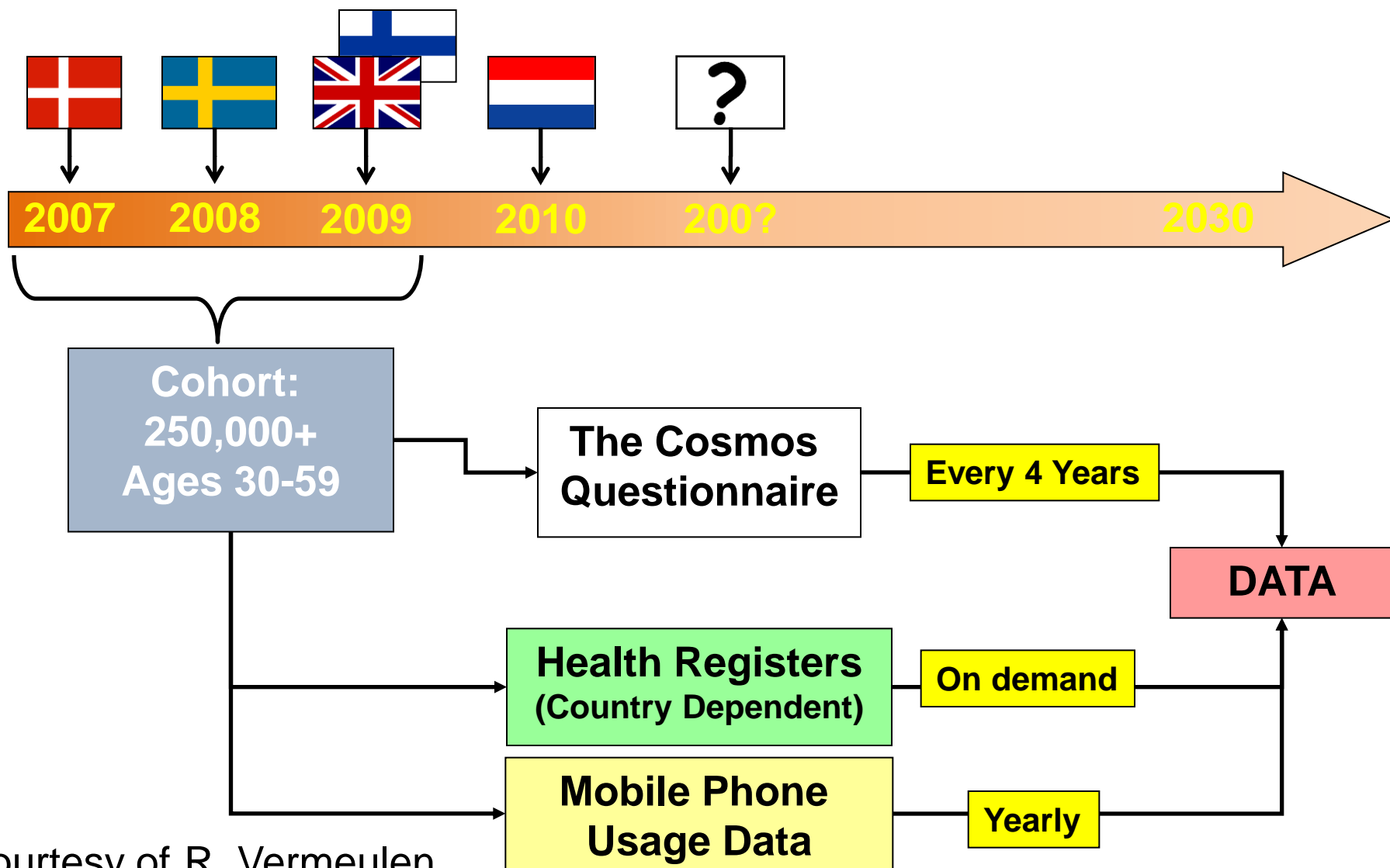
Finland



Netherlands



U.K.



Main Health Endpoints

Main health outcomes	
Cancer	Malignant brain tumors
	Benign brain tumors (including acoustic neuromas)
	Breast cancer
	Hematopoietic cancers
Neurological	Alzheimer's
	Parkinson's
	Amyotrophic Lateral Sclerosis
	Multiple Sclerosis
Other diseases	Cardio/cerebrovascular diseases
Non-specific symptoms	Memory problems (e.g., dementia)
	Parkinson-like symptoms
	Depressive symptoms
	Sleep problems, fatigue, headache, tinnitus, etc
	General health (HRQoL)

Cosmos: Advantages & Disadvantages

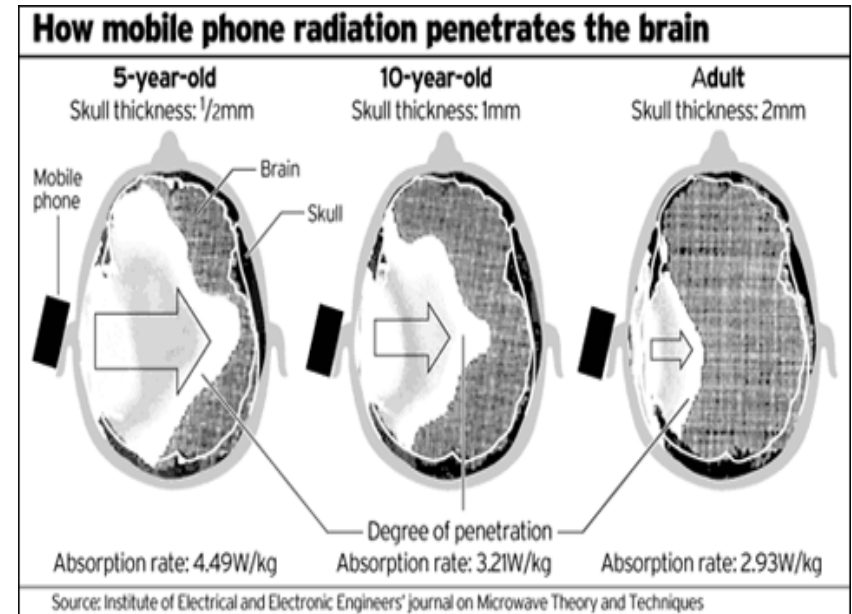
Advantages	Disadvantages
Improved exposure assessment	Large populations needed to study rare outcomes
Multiple endpoints	Attrition (loss of participation)
Rapid assessment of new hypotheses	

Courtesy of R. Vermeulen



Cell Phone Use & Childhood Cancer: Rationale

- Greater susceptibility of developing nervous systems
- Greater penetration of RF relative to head size
- Longer exposure than adults
- Only 1 epidemiologic study
- Ongoing childhood cohort studies (N=200,000)



Childhood Cell Phone Use & Brain Tumor Risk*

- Population:
 - > incident tumors ages 7-19, Denmark, Norway, Sweden, Switzerland
 - > 352 cases (83% participation) vs. 646 controls (71% participation)
- Exposure assessment:
 - > questionnaires to children and parents & operator records
- Results:
 - > no association with regular use, duration of use, cumulative use or side of head where phone held; ↑ risk with time since 1st use
- Conclusion: little evidence of a relationship

MOBI-Kids



mobi-kids

Study on Communication Technology,
Environment and Brain Tumours in Young People

Courtesy of R. Vermeulen

<http://www.mbkds.com>



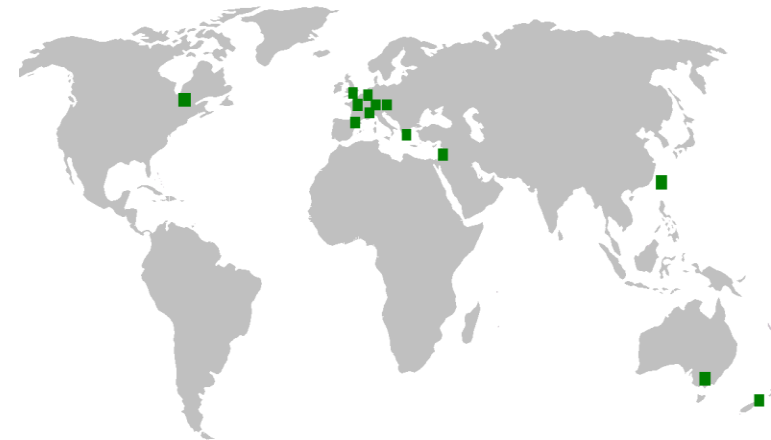
Objectives

- Overall objective
 - To assess the potential tumorigenic effects of childhood and adolescent exposure to RF and RF from mobile telephones on tumours of the central nervous system

... build upon the methodological experience of
INTERPHONE

Study Design

- Case-control study
 - Cases (~2000)
 - benign and malignant brain tumours
 - ages 10-24
 - rapid ascertainment
 - Controls
 - 2 per case
 - hospital-based, to minimize selection bias related to non-participation
 - individually matched on age, sex, region
 - Estimated publication 2016



Will Ongoing Epidemiologic Studies Clarify Whether Cell Phone Use Increases Cancer Risks?

<http://www.cancer.gov/about-cancer/causes-prevention/risk/radiation/cell-phones-fact-sheet>

<http://www.cancer.gov/about-cancer/causes-prevention/risk/radiation/electromagnetic-fields-fact-sheet>