



# The rationale of the 2B IARC classification for RF Fields

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*The control of physical agents,  
Novara, 07 may 2012*

# Radio-frequency fields

- Electromagnetic fields - 30 kHz–300 GHz
- Workers: high power sources (induction heaters, radars) can have higher cumulative whole body exposure
- Mobile phone users: higher brain exposures
- Base stations: exposures lower

# Epidemiological studies on cancer risk and RF

- Occupational studies
- Mobile phone studies
  - Incidence time trends studies
  - Cohort studies (Danish cohort)
  - Case control studies (Interphone and “Hardell” studies)

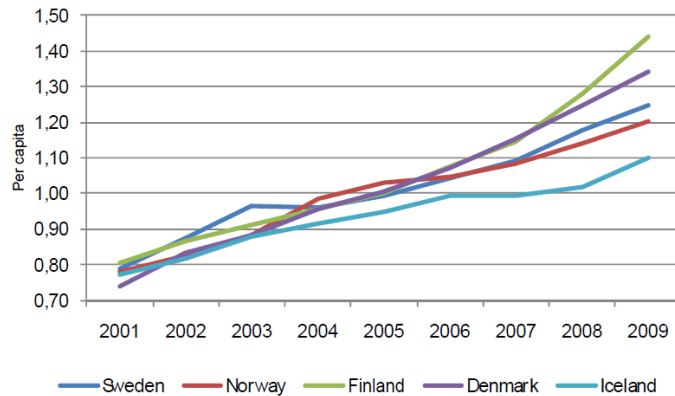
# Incidence time trends studies

- Yearly description of number of new cancer cases (after age standardisation to a reference population) occurring in a population
- Based on cancer registry data
- Informative for effects occurring at population scale
  - Screening programmes, introduction of new diagnostic tools, impact of tobacco epidemic
- Not informative for effects occurring in small subgroups of population, or if other factors are also changing at population scale

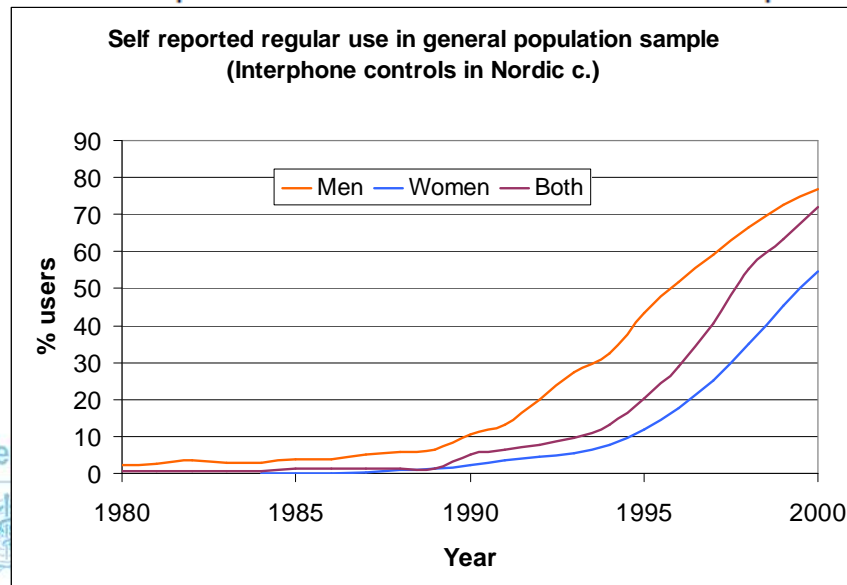
=> If mobile phone use causes gliomas, it will ultimately show up in incidence rates of this disease

# Prevalence of use of mobile phones (Nordic countries)

Mobile subscriptions<sup>1</sup> per capita



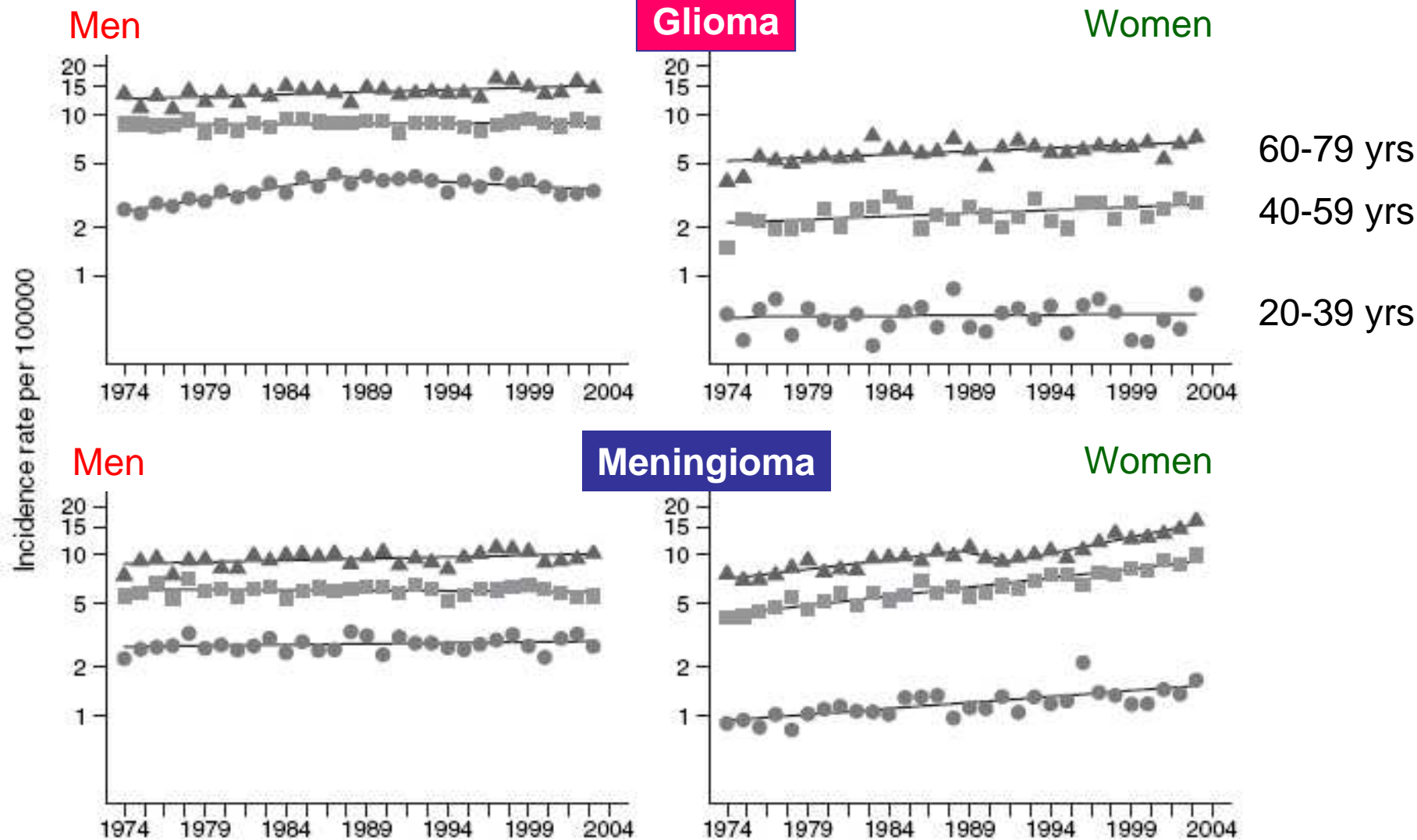
<sup>1</sup>Includes both private and business GSM/UMTS subscriptions.



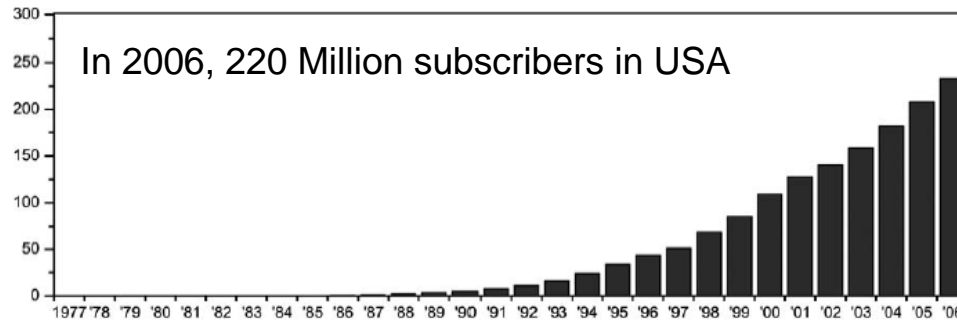
- Very similar between Nordic countries
- Differences in prevalence of use at given time between age and gender groups
- Men aged 40-60 yrs first to adopt mobile phones

# Incidence rates of brain tumors (Nordic countries - 2003)

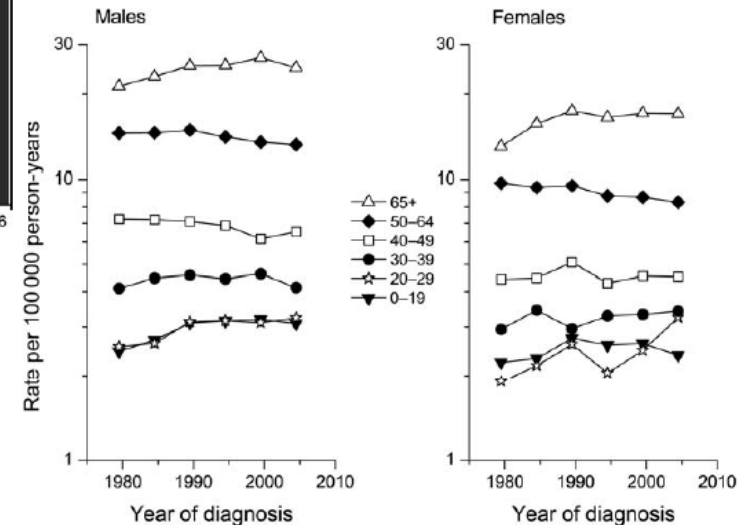
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# Incidence time trends of malignant brain tumours



USA, 1977-2006 – 10 % of total pop.



n cancer incidence trends among whites by age, SEER 9, 1977–1981 to 2002–2006.

*Inskip et al, Neurology, 2010*

England,  
1998-2007

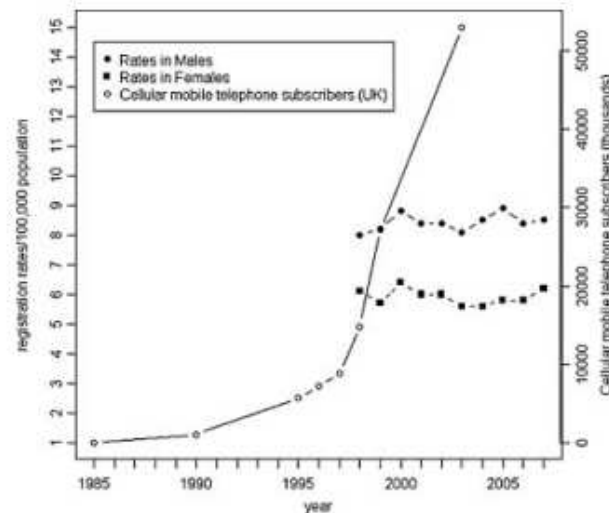


Fig. 1. Brain cancer incidence rates between 1998 and 2007 per 100,000 people in England and number of mobile phone subscribers in the UK between 1985 and 2003 [ITU, 2010].

*de Vocht et al, Bioelectromagnetics, 2011*

# Incidence studies

- Provided evidence that there is no observable effect of mobile phones at the population scale on glioma in 3 different studies (6 countries) up to 2003, 2006, 2007
- Could miss an effect if effect was small, limited to small subgroups (highest users, temporal lobe tumors) or occurred at the population scale after longer time than observed so far

Stresses the importance of high quality cancer registration for epidemiological studies



# Cohort studies

- Follow a group of people over time
- Compare the occurrence of disease among exposed individuals to non-exposed individuals

# Danish cohort of early mobile phone subscribers: design

From the 2 danish mobile telephone companies , Sonofon and TeleDanmarkMobil, all numbers issued between 1982 and 1995 were obtained, name and address of subscription holder (person or company), date of subscription



Exclusions:

200 000 corporate subscriptions (no individual user identified)  
100 000 subscriptions (mismatches -names or addresses, 2 subscriptions for same name,...)

Identification of 420 095 persons early subscribers of mobile phones and their date of subscription (1982-1995)

# Danish cohort study: results for follow-up to 2002

- Mean exposure duration: 8.5 years
- Number of cases : glioma 257, meningioma 68
- Results :
  - Entire follow up, gliomas: SIR=1.01 (0.89-1.14)
  - 5-9 years, all CNS, men : SIR= 0.96 (0.84-1.09)
  - 10+ years all CNS, men : SIR= 0.66 (0.44-0.95)
- But
  - number of cases small
  - No information on level of use

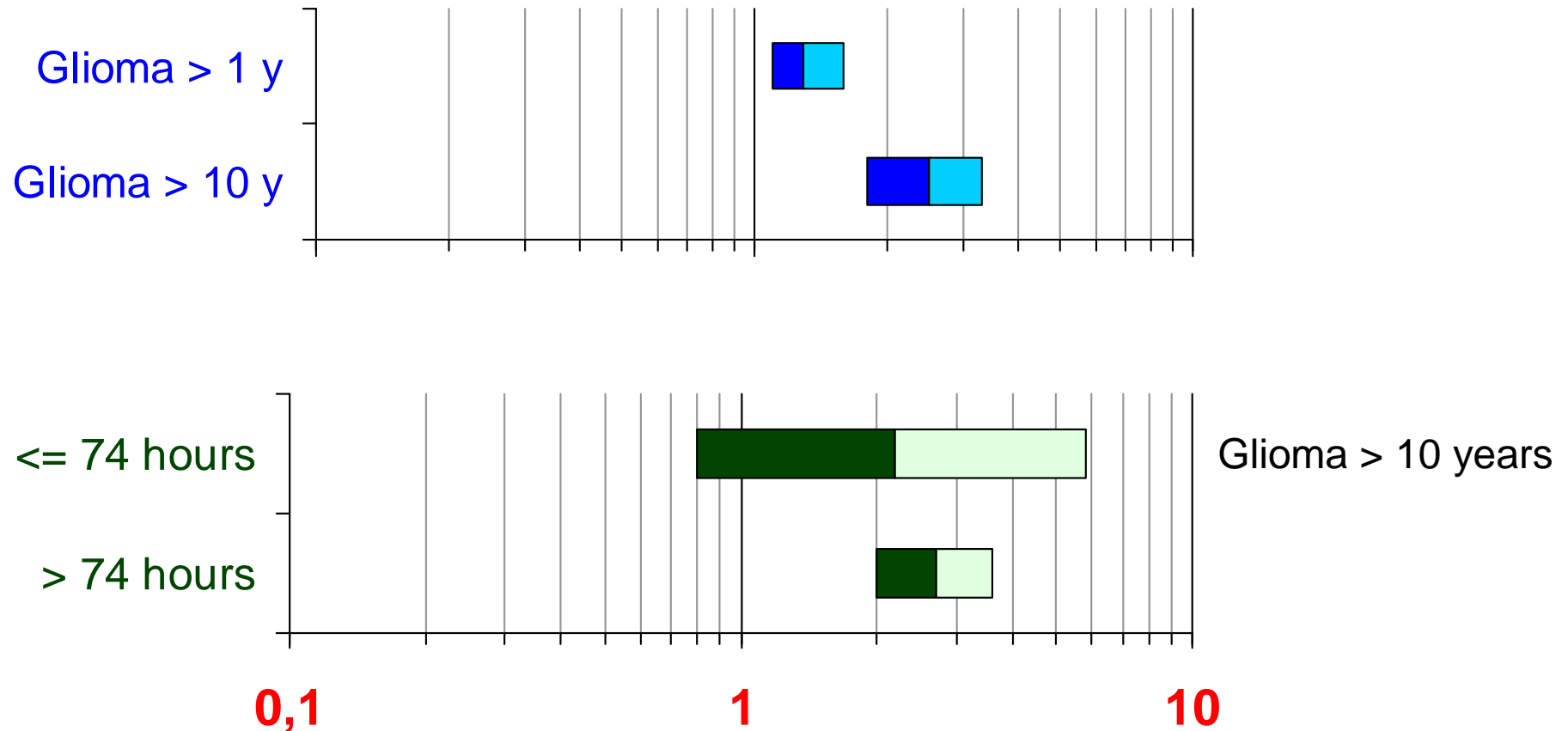
*Schüz et al, J Natl Cancer Inst, 2006*

# Case-control studies

- Comparison of past exposures of
  - Individual with disease (cases)
  - Random sample of population (controls)
- Quality of case-control study
  - High participation ensures no selection bias (cases and controls representative of the same source population)
  - Assessment of exposure is important
    - Random error in exposure -> underestimation of association exposure - disease
    - Recall bias is a concern (cases report differently than controls)

# Case-control studies

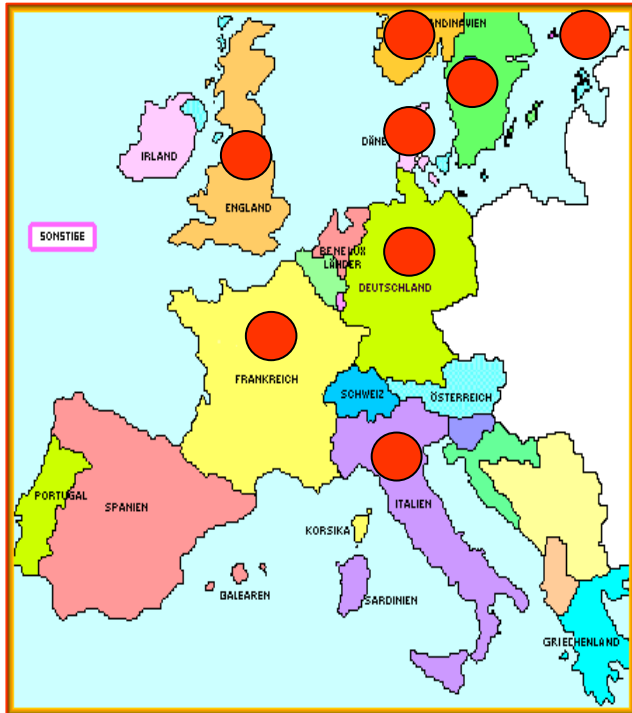
Case-control studies in Sweden, by Hardell and team:



# Interphone Study

Cardis et al., Eur J Epidemiol, 2007

16 centers in 13 countries  
European centers



+ Australia, Canada, Israel,  
Japan, New Zealand

**Study of mobile phone use and  
risk of brain tumours and acoustic  
neuroma among adults (30-59  
years old).**

**Characteristics:**

*Personal interviews with:*

- 2708 patients with glioma
- 2409 patients with meningioma
- 1105 patients with ac. neuroma
- similar number of controls  
or their proxies

Ascertainment: 2000-2003

# Representativity of the control population

## Recall of mobile phone use

- Low response rate among controls (53%)
- More mobile phone users among participants than among non-participants

672 volunteers in 11 countries

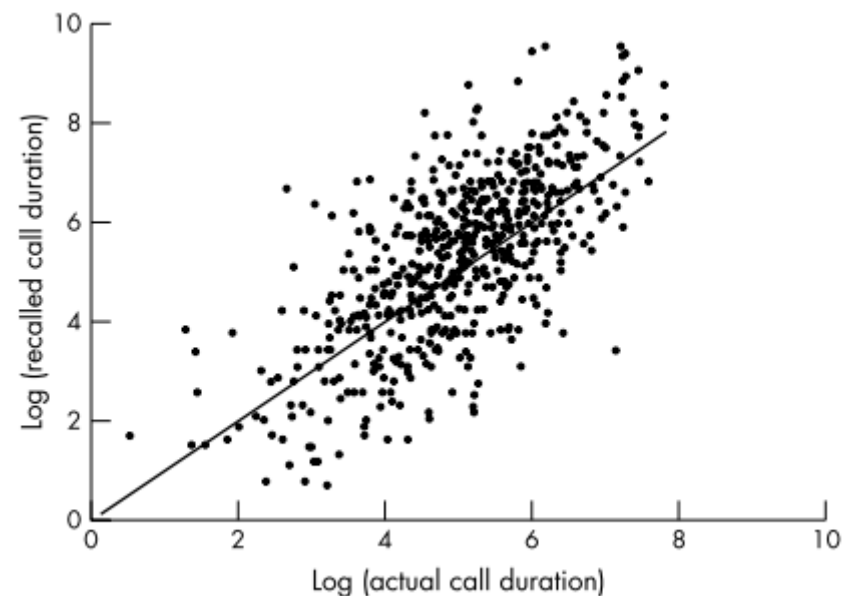
Actual duration of use: Operators or Software V

Recalled use: questionnaire

Ratio: recalled to actual monthly  
duration of calls  
mean = 1.4

95% of subjects:  $0.12 < \text{ratio} < 17$

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*Vrijheid et al, OEM, 2006*

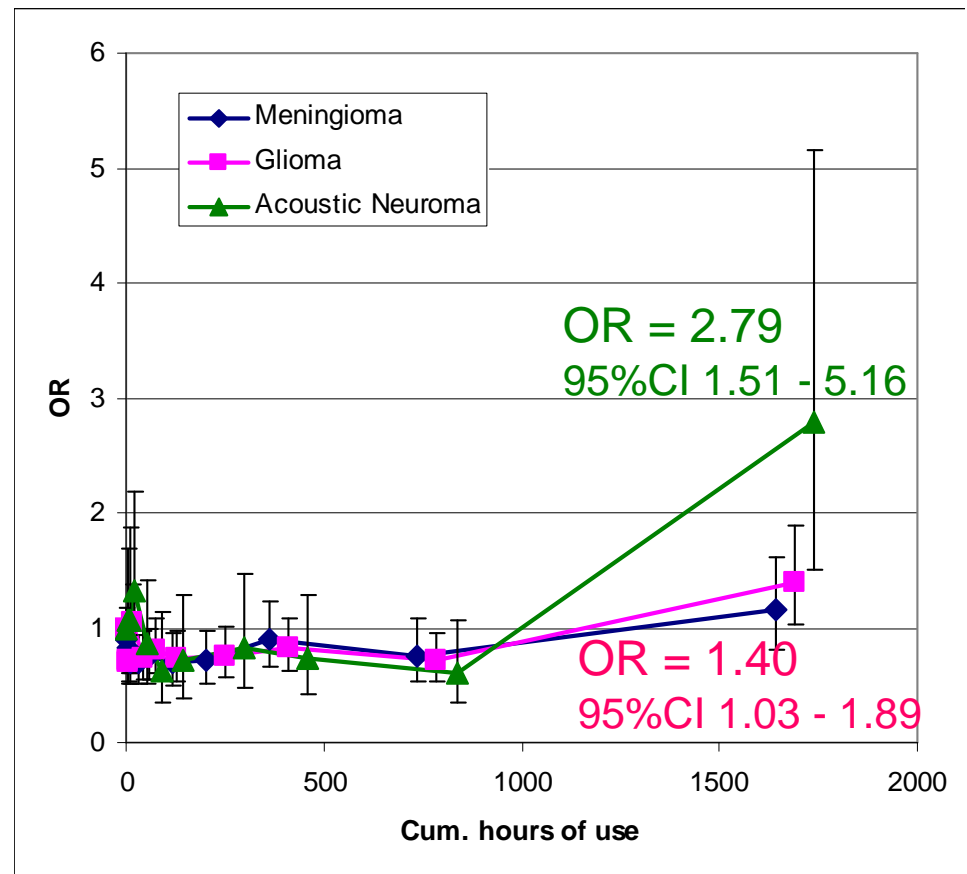
# Interphone (all countries): results

*Interphone Study Group, Int J Epidemiol, 2010*

*Interphone Study Group, Cancer Epidemiol, 2011*

- For meningiomas, no increased risks
- For gliomas and acoustic neuromas:
  - No increased risk for the majority of users
  - for the 10 % highest user group Increased risks of glioma and acoustic neuroma (5 year latency)

Biases and errors prevent a causal interpretation





# IARC Monograph program

2 to 3 times per year, ad hoc group of expert convenes for 1 week

- Review published literature
  - Sources and Exposure mechanisms
  - Studies of carcinogenicity in humans (epidemiology)
  - Studies of carcinogenicity in animals (in vivo)
  - Other relevant data (in vitro, ...)

# Classification scheme

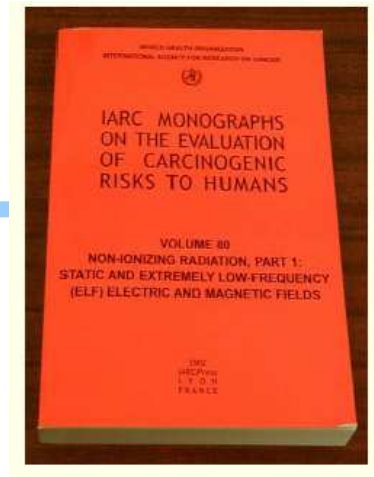
- 1 – carcinogenic to humans (tobacco, HPV virus type 16, ionising radiation, benzene, ethanol in alcoholic beverages...)  
*Sufficient evidence in humans: causal relationship has been established, in which chance, bias and confounding could be ruled out*
- 2a – probably carcinogenic to humans: limited evidence in humans, sufficient evidence in animals (emission from high temperature frying, shift work,...)  
*Epidemiological studies: causal interpretation is credible, but chance, bias and confounding could not be ruled out as possible explanations.*
- 2b – possibly carcinogenic to humans: limited evidence in humans, not sufficient evidence in animals (chloroform, dry cleaning, naphthalene,... )  
*Epidemiological studies: causal interpretation is credible, but chance, bias and confounding could not be ruled out as possible explanations.*
- 3 – not classifiable: inadequate data (aciclovir, eosin, haematite, personal use of hair colouring products,...)
- 4 – evidence of lack of carcinogenicity (1 agent)

# Conclusions

Time trends in incidence rates of brain tumours  
*... show no increase suggesting a mobile phone-related effect*  
*... would not show small effect in longer term heavy users yet*

## Cohort study

*... does not show an increased brain tumour risk*  
*... did not allow any investigation by amount of use*



24-31 May 2011  
IARC Monograph

## Case-control studies

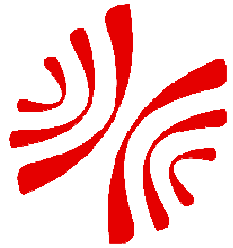
“Although both INTERPHONE and Swedish pooled analysis are susceptible to bias—due to recall error and selection for participation—the Working Group concluded that the findings could not be dismissed as reflecting bias alone, and that a causal interpretation between mobile phone RF-EMF exposure and glioma is possible. A similar conclusion was drawn from these two studies for acoustic neuroma,...” -> limited evidence from epi studies

Few members: inadequate evidence from epi studies

(lack of dose response in Interphone, inconsistencies between C-C studies, lack of effect in other epidemiological studies)

# New publications since May 2011

- Cefalo study: Brain tumours in children and adolescents (July 2011)
- Update of Danish cohort study with cancer cases occurring up to 2007 (Nov 2011)
- 2 Incidence studies of glioma (Nordic countries, USA) up to 2008 – comparison of trends with OR from case-control studies (Jan 2012, Mar 2012)



## Cefalo: Children & Teenagers Brain Tumor

*Aydin et al, J Natl Cancer Inst, 2011*

- International case – control study among 7-19 year in Denmark, Norway, Sweden and Switzerland (352 cases-646 controls)
- Use of mobile phones : Self reported + operators records if available
- Results:
  - OR (user/non user)= 1.36; (95% CI = 0.92 to 2.02)
  - Significant trend with increasing time based on Operators records (163 subjects). OR (>2.8 y) = 2.15 (1.07 to 4.29)
  - Inconsistent results with laterality, tumor location
- Need for further studies with good exposure information
- Need of monitoring of incidence time trends

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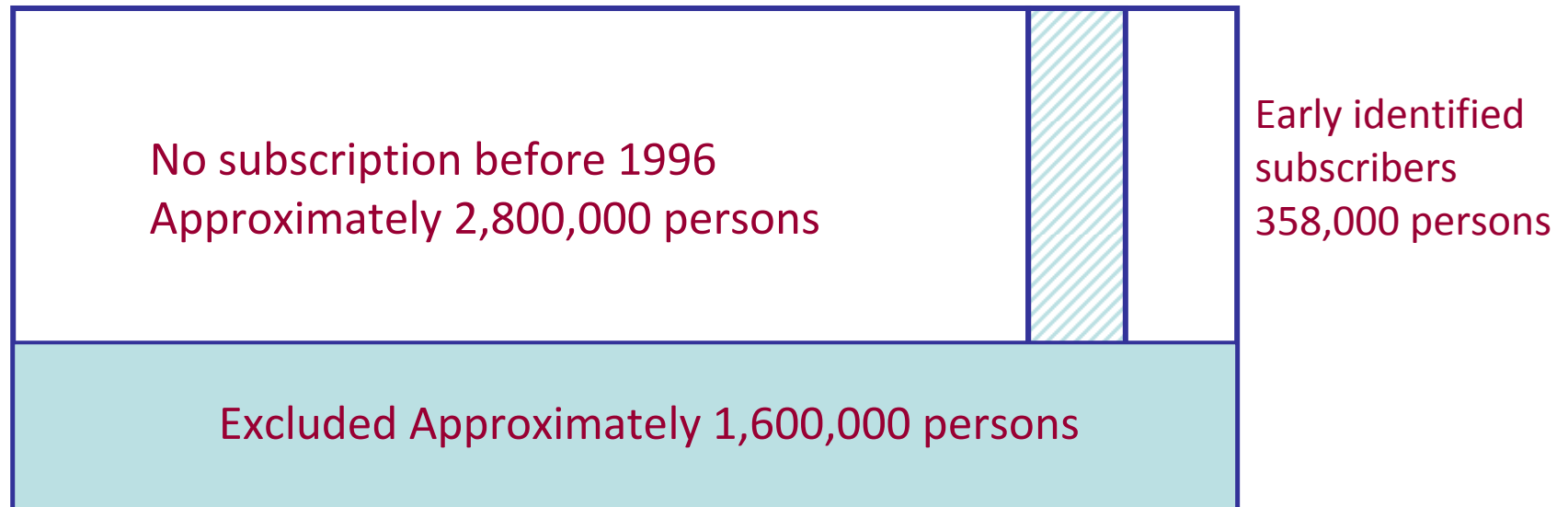


# Danish cohort: updated analyses to 2007

*Frei et al, BMJ, 2011*

Exclusion of subscriptions contracted prior to 1987 (mainly car phones)

Link with individual data on income, education available for all Danes born after 1925, older than 30, after 1990.



 Not identified subscribers

Analysis: observed versus expected cases Stratified by sex, age, calendar period, education, income

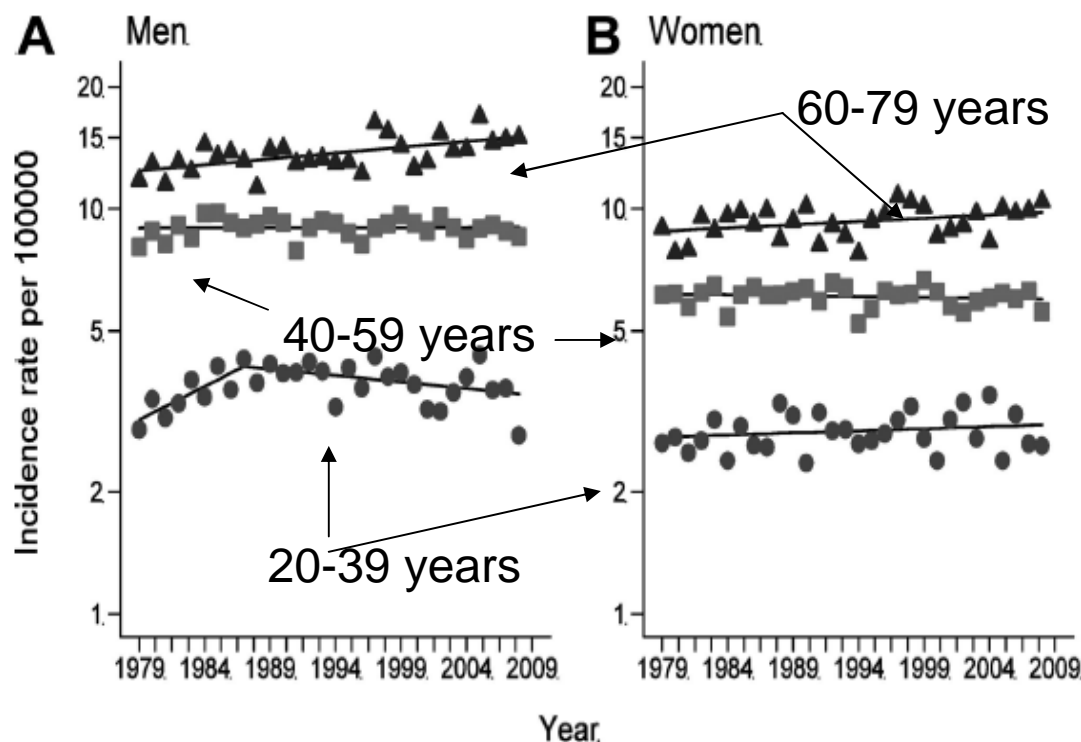
Results: 356 glioma cases among early subscribers,

Men gliomas - 10-12 years: IRR=1.06 (0.85-1.34)

Men gliomas  $\geq 13$  years: IRR=0.98 (0.70-1.36)

## Glioma incidence rates in Denmark, Finland, Norway and Sweden (1979-2008)

*Deltour et al, Epidemiology, 2012*



- 35,250 cases among  
510 million person-years  
at risk

- change in IR per year:  
0.4% men, 0.3% women

Evaluation of predicted increases in IR based on Increased OR in case-control studies and compatibility with time trends

(Hardell) OR(>10 y)  $\approx 2$  is **100% inconsistent**

**=> biases and errors in self reported use leading to spuriously high ORs**

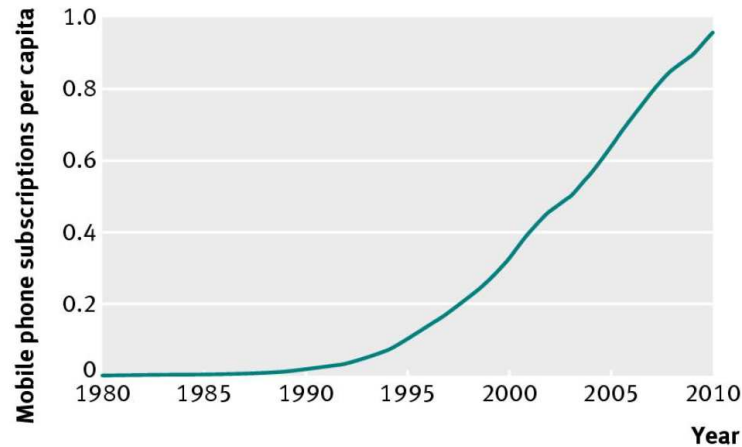
(Interphone) OR(heavy us)  $\approx 1.5$  is **98% inconsistent ; 2% consistent**

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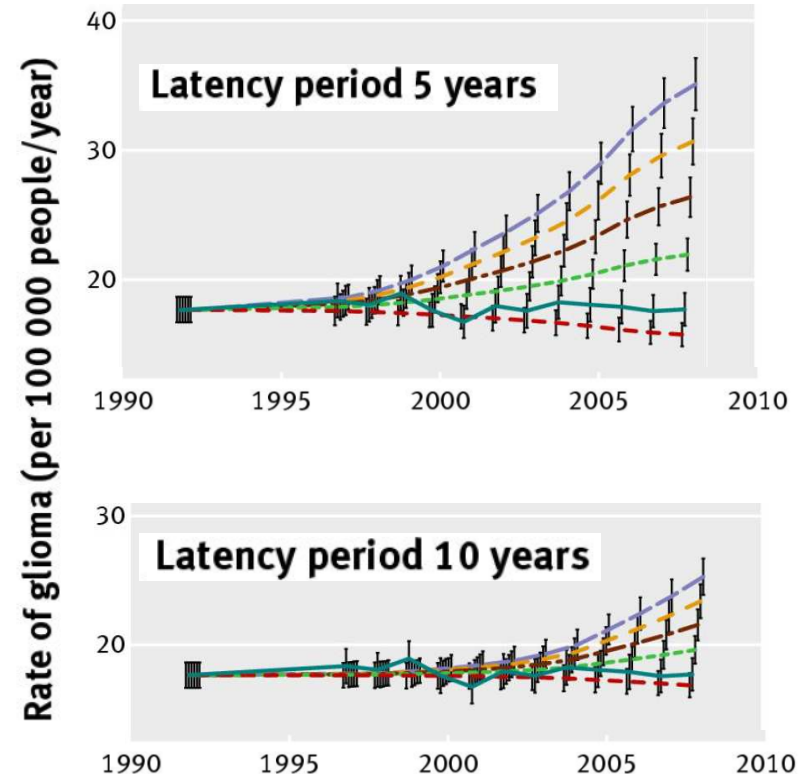
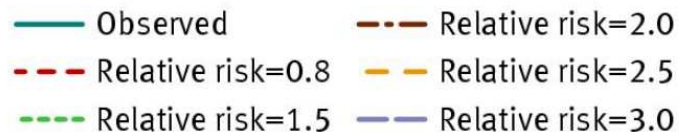


## Glioma incidence rates in USA (1992-2008)

*Little et al, BJC, 2012*



**Fig 1** Mobile phone subscriptions per capita in the US, by year



12 registries in USA, 24,813 glioma cases 18 yrs+,

Evaluation of consistency of incidence rates with published OR

- $OR(>10\text{ y}) \approx 2$  (Hardell) **100% inconsistent**

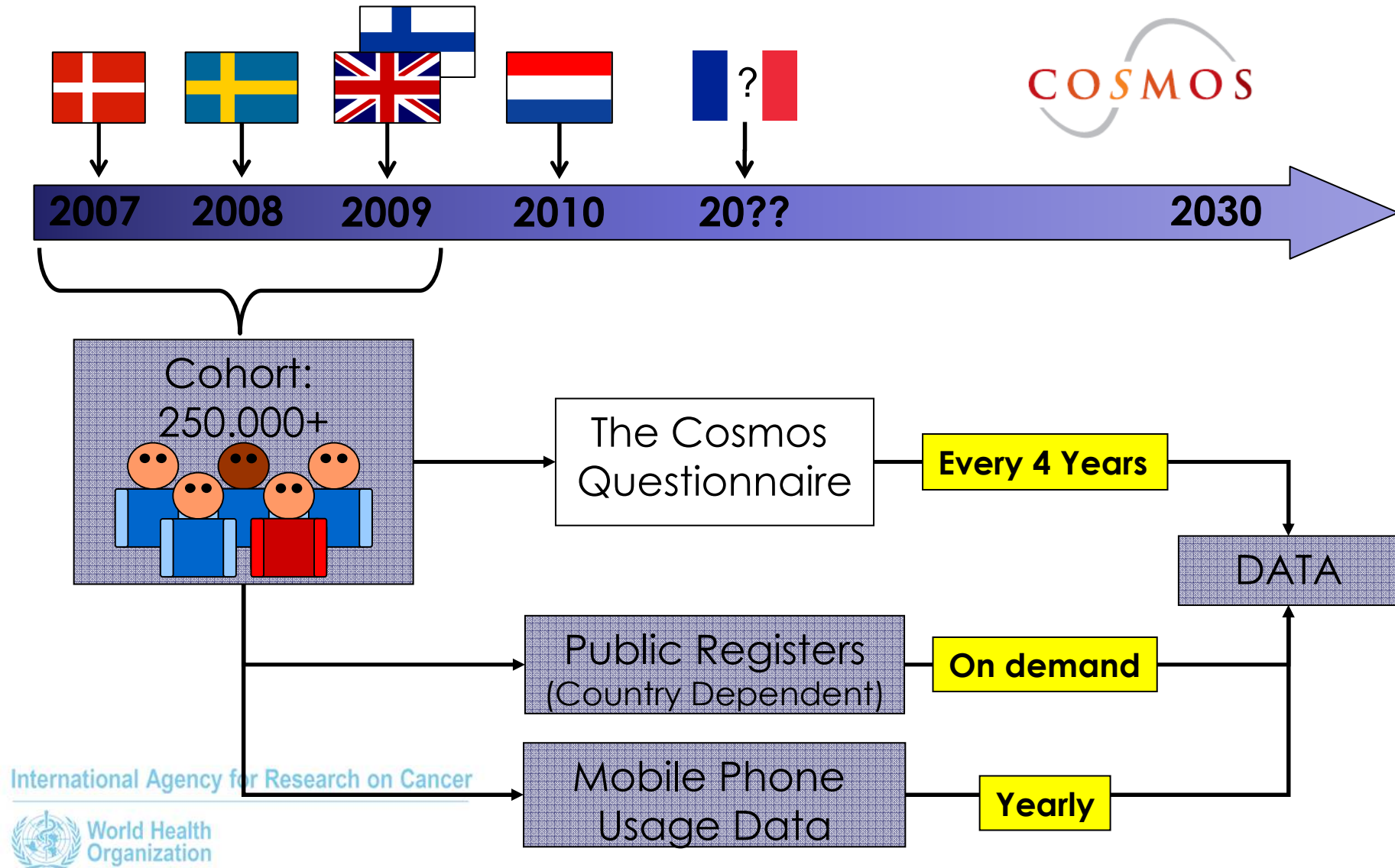
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# COSMOS:

*Schüz et al, Cancer Epid, 2010*

International Cohort Study of Mobile Phone Use and Health



- Thank you for your attention

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