

Epidemiological studies on HF

Maria Feychting

ICNIRP Vice Chair

Professor of Epidemiology

Institute of Environmental Medicine

Karolinska institutet, Sweden

Epidemiological studies – strengths and limitations

Strengths

- Conducted in the relevant species – i.e. humans
- Relevant environment –
 - Adequate exposure circumstances
 - Adequate effect modifiers present

Limitations

- In studies of non-reversible adverse effects –exposure cannot be controlled by the scientist
 - Various sources of bias may be present to greater extent than in experimental studies
 - Confounding
 - Exposure misclassification
 - Selection bias

Epidemiological study designs

- Hierarchy of study designs:
 1. Cohort studies with prospectively registered exposure information
 - Minimizes recall bias and selection bias
 - Drawback: Often crude exposure assessment
 2. Case-control studies
 - More detailed exposure assessment – however, often rely on retrospectively self-reported information – **recall bias** is a problem
 - Control selection and non-participation may lead to selection bias
 3. Cross-sectional studies
 - Often not useful for assessment of causality
 - Affected by: selection bias, recall bias, reverse causation

Cancer – brain tumors

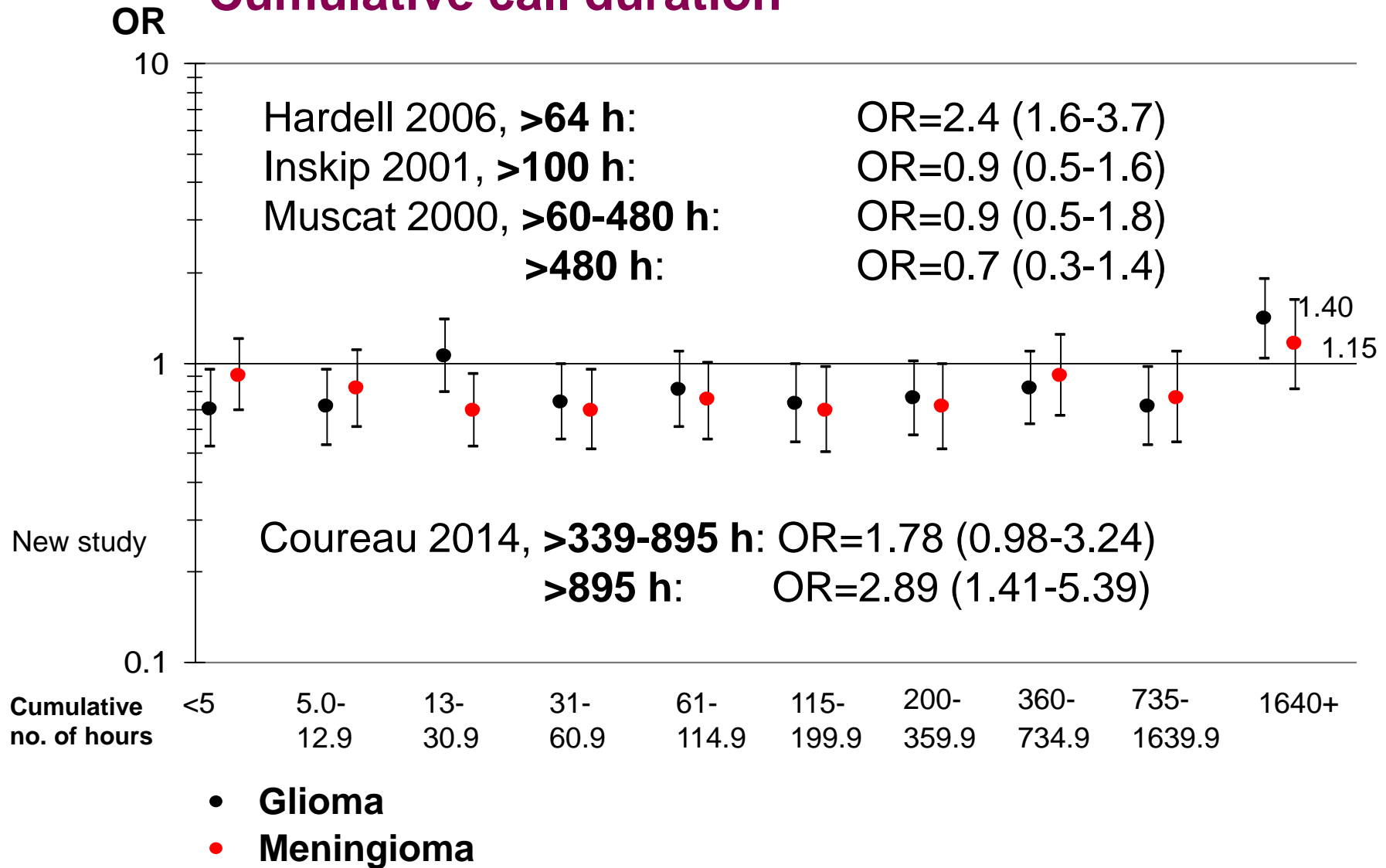
- Radiofrequency electromagnetic fields was classified by IARC in 2011 as “possibly carcinogenic to humans” (Group 2B), a category used when a causal association is considered credible, but when chance, bias or confounding cannot be ruled out with reasonable confidence
- Major biases discussed:
 - Selection bias in case-control studies from non-participation leads to underestimation of risk
 - Recall bias in case-control studies – cases tend to over-report mobile phone use in distant past, leads to over-estimation of risk
- It was also noted that incidence trends did not support a risk increase, but studies available covered only a short time period when the evaluation was made

New evidence since the IARC evaluation

- A few new case-control studies with retrospective recall of phone use, some report increased risks – potential recall bias, implausible results
 - E.g. one study reports more than 3-fold risk increase for >25 years of mobile phone use – however, handheld mobile phones had only been available for max 23 years
 - Results not compatible with incidence trends worldwide
- New analyses of Danish cohort study of subscribers
 - No associations with long-term use
- One new cohort study from the UK with prospectively collected information on mobile phone use – no recall bias
 - No association with long-term or daily use
- First study on brain tumors in children found no increased risk related to mobile phone use

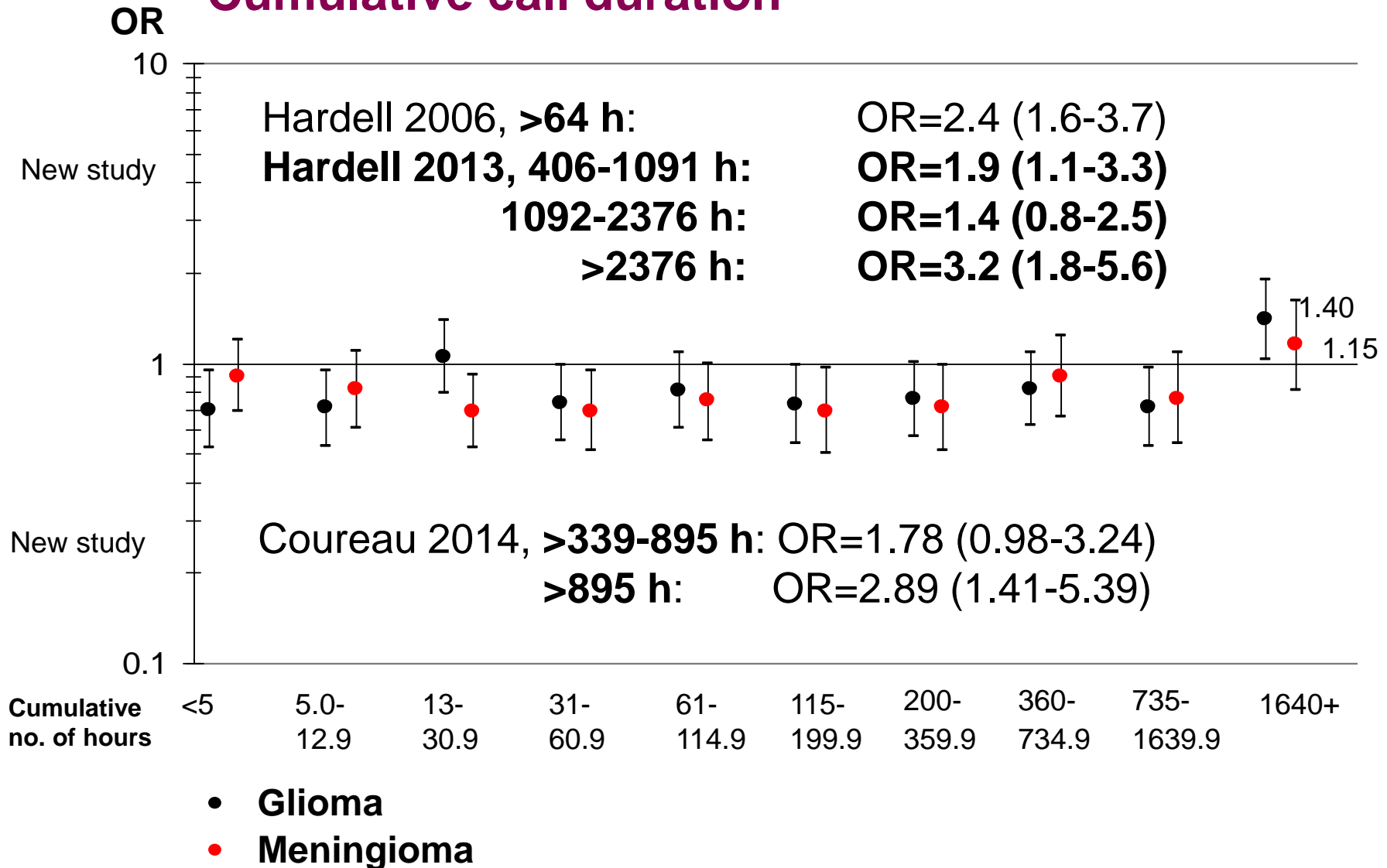
Interphone results brain tumors

Cumulative call duration



Interphone results brain tumors

Cumulative call duration



New evidence since the IARC evaluation

- Brain tumor incidence trend studies with much longer follow-up are now available from many countries
 - No indications of increased glioma incidence – worldwide

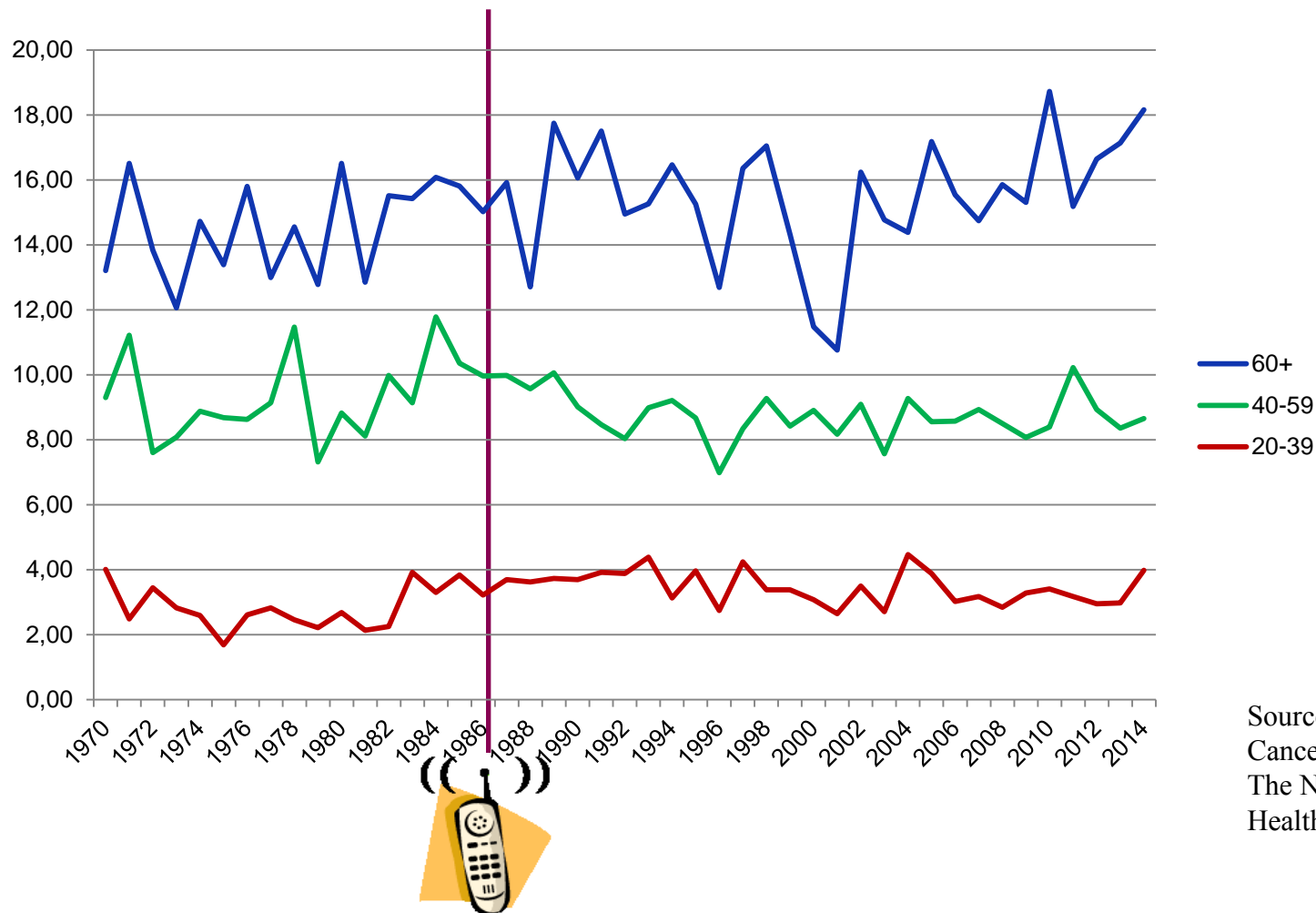
UK: Age specific brain cancer incidence trends 1998-2007, de Vocht et al., Bioelectromagnetics, 2011

- The study by de Vocht et al. shows incidence trends for malignant brain tumors during the period 1998-2007 in different age groups
- No increase in the brain cancer incidence since the introduction of mobile phones was seen.

Glioma incidence, Sweden 1970-2014, Men

per/100 000
age standardized

Introduction of handheld
mobile phones



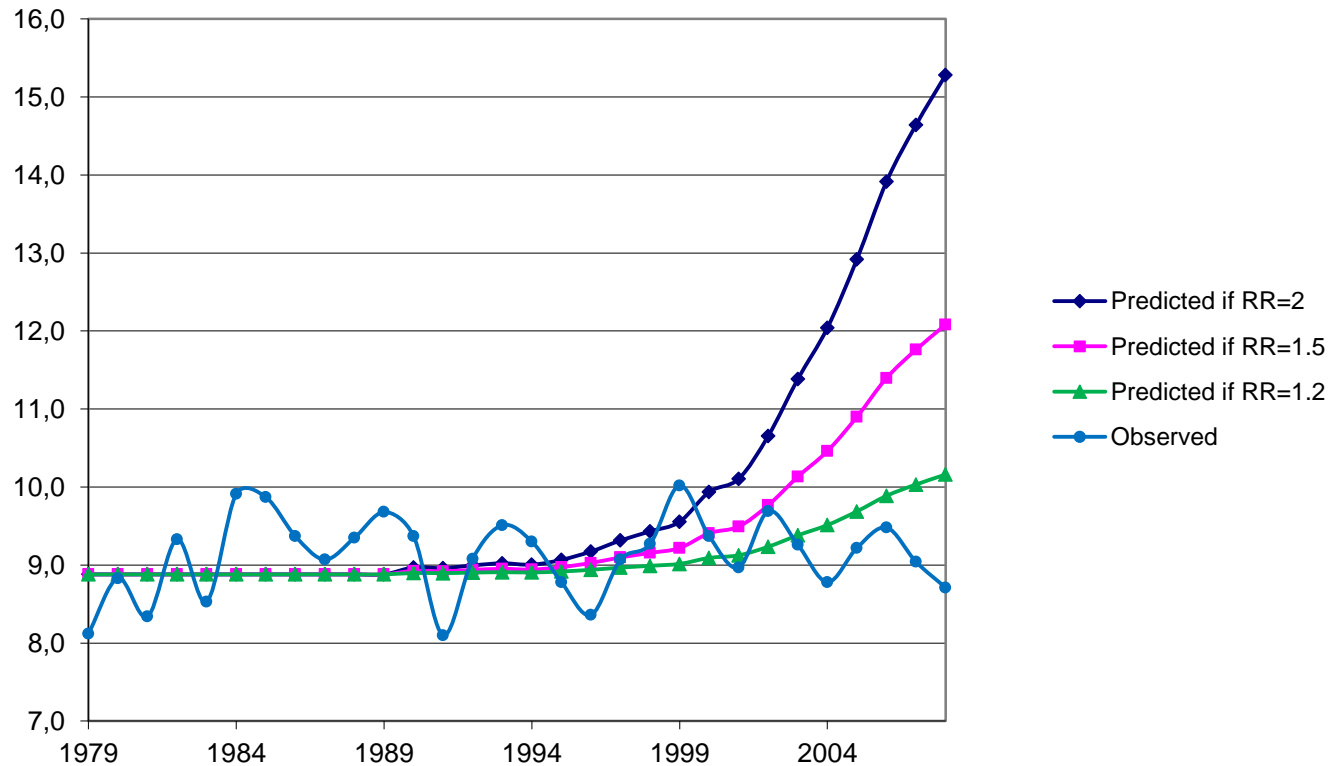
Source:
Cancer Register,
The National Board of
Health and Welfare

New evidence since the IARC evaluation

- Simulation studies – estimated what the incidence would have been if results from some case-control studies were true
 - Deltour et al. 2012, Nordic countries
 - Little et al. 2012, The UK
 - Chapman et al. 2016, Australia

Observed and predicted glioma incidence rates under scenarios of risk, Nordic countries, men 40-59 years, 1979-2008

Under the assumption that all users at increased risk after 10 years:



Observed and expected brain cancer incidence rates in Australia

Chapman et al., Cancer Epidemiology, 2016, estimate the incidence trend for brain cancer that would have been expected if the relative risk associated with at least 10 years of mobile phone use would be 1.5, i.e. a 50% increased risk,

and also if a relative risk associated with heavy mobile phone use would be 2.5.

If any of these scenarios would be true, the incidence of brain cancer would have increased considerably in the age groups where mobile phone use have been common, and would have been clearly visible in the incidence trend.

The observed incidence, however, has not increased at all in these age groups. The incidence has increased among persons over 70 years old, and this increase started before the introduction of mobile phones, likely because of greater availability of improved diagnostic methods such as CT and MRI.

Symptoms and wellbeing

- Investigated outcomes are e.g. headaches, sleeping problem, fatigue, loss of appetite, concentration problems
- Most epidemiologic evidence is from cross-sectional studies – often self-reported outcome and self-reported exposure
 - Nocebo effects, recall bias, selection bias, and confounding are major concerns
- No associations reported when exposure was independently measured
- Only one prospective cohort study available – found no associations – but only one year of follow-up
- Overall, results do not support the hypothesis that RF exposure causes non-specific symptoms.

Behavioral outcomes – cross-sectional studies

- Mobile phone use is part of a lifestyle, which may be associated with various outcomes
- Behavioral problems may be associated with a certain lifestyle
 - Likely to increase own mobile phone use
- May lead to false positive results
 - Behavioral problems may increase mobile phone use rather than the opposite
- Difficult to determine when the condition started
 - Reversed causality potential problem also in cohort and case-control studies with insufficient latency period

Maternal exposure during pregnancy – behavior

- Effects on behavioral problems at age 7, reported in two publications from a Danish cohort study
 - Divan et al. 2008, Divan et al. 2010
 - Retrospective self-reported assessment of mobile phone use
- Both publications report increased risk
 - Highest risk with both prenatal and postnatal phone use – combined OR=1.5 (95% CI 1.4-1.7)
 - Strong hereditary component – mothers who were early mobile phone users possibly different
 - Extensive confounding control
 - Children born 1998-2001 – lower risks in more recent birth cohorts – residual confounding?

Maternal exposure during pregnancy - behavior

- A Dutch study could not confirm the findings in the Danish cohort study - Guxens et al. 2013
 - Children born 2003-2004
- RF exposure of the fetus from maternal mobile phone use is likely to be extremely low – effects implausible
 - Other hypotheses: Maternal mobile phone use draws attention from the child?
 - Confounding from other exposures related to a lifestyle which also includes extensive mobile phone use

Reproductive outcomes

- Some studies have indicated an effect on sperm quality
 - Cross-sectional studies with recruitment of patients at fertility clinics – not representative samples
- Studies of occupational exposures have not found consistent effects on fertility or other reproductive outcomes
 - Poor exposure assessment
 - Multiple comparisons
- The data available are not of sufficient quality

Conclusions from epidemiology

- **No substantiated evidence of adverse health effects from RF exposure at levels below current guidelines**
- Evidence on mobile phone use and glioma has become considerably weaker since the IARC evaluation
- Does not support the hypothesis that RF exposure causes non-specific symptoms
- Results on behavioral problems are inconsistent
- Studies on fertility and other reproductive outcomes are of poor quality