Overview:
Radiofrequencies and cancer

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Radiofrequencies and Health:
Research in a fast-moving environment
IARC CLASSIFIES RADIOFREQUENCY ELECTROMAGNETIC FIELDS AS POSSIBLY CARCINOCENIC TO HUMANS

Lyon, France, May 31, 2011 -- The WHO/International Agency for Research on Cancer (IARC) has classified radiofrequency electromagnetic fields as possibly carcinogenic to humans (Group 2B), based on an increased risk for glioma, a malignant type of brain cancer, associated with wireless phone use.
### IARC Monographs Programme approach

<table>
<thead>
<tr>
<th>Step</th>
<th>Task</th>
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<tbody>
<tr>
<td>1</td>
<td>Identify relevant information</td>
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<tr>
<td>2</td>
<td>Screen, select &amp; organize studies</td>
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<tr>
<td>3</td>
<td>Evaluate study quality</td>
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<td>4</td>
<td>Report study characteristics</td>
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<tr>
<td>5</td>
<td>Synthesize evidence→ overall evaluations</td>
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#### Overall evaluations:
- Synthesize findings in 3 evidence streams
- Categorize each line of evidence using defined terms

### Cancer in humans
- Sufficient evidence
- Limited evidence
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity

### Cancer in experimental animals
- Sufficient evidence
- Limited evidence
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity

### Mechanistic and other relevant data
- Strong evidence
  - Mechanistic class
  - Key characteristics
  - Mechanism not relevant
- Limited evidence
- Inadequate evidence

### Overall evaluation
- **Group 1** Carcinogenic to humans (122)
- **Group 2A** Probably carcinogenic to humans (93)
- **Group 2B** Possibly carcinogenic to humans (319)
- **Group 3** Not classifiable as to its carcinogenicity to humans (501)
Artificial UV from sunbed use is carcinogenic to humans

1.8% increase in melanoma risk with each session of sunbed use per year

For France in 2015, 382 cases of melanoma were estimated to be attributable to use of sunbeds and could have been prevented

Arnold et al., J Eur Acad Dermatol Venereol, 2018
Boniol et al., BMJ, 2012
16 centres in 13 countries
Ascertainment: 2000-2003
Coordinated by IARC/WHO

INTERPHONE Study

Interphone Study Group, Int J Epidemiol, 2010
Interphone Study Group, Cancer Epidemiol, 2011
**Individual risk of developing a glioma by hours of use of mobile phones cumulated over the entire lifetime (30-59 year olds between 2000-2003)**

*Population risk:*
- about half of the population were never regular users of a mobile phone (reference group)
- almost half of the population had no increased (or slightly decreased) risk
- about 5% of the heaviest lifetime mobile phone users had moderately increased risk

*Interphone Study Group, Int J Epidemiol, 2010*
Cohort Studies (Denmark, UK (Women))

**Individual risk from comparing the earliest subscribers for a mobile phone in Denmark (before 1995) with the rest of the Danish adult population**

**Individual risk from comparing never mobile phone users with mobile phone users by number of years of use within UK Million Women Study**

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**Years of subscription**

- Never
- 1 to 4
- 5 to 9
- 10+

**Years of mobile phone use**

- Never
- < 5
- 5 to 9
- 10+

**Frei et al., BMJ, 2011**

**Benson et al., Int J Epidemiol, 2013**
New studies after 2011 – Animal data?

Carcinogenic hazard in rats (Ramazzini study):
~19 hrs of exposure each day with varying levels 0.001-0.1 W/kg

Increase in heart schwannoma in male rats at highest dose
No increase in female rats

Falcioni et al., Environ Res, 2018

Carcinogenic hazard in rodents (NTP Studies):
~9 hrs of exposure each day with varying levels between 1.5 – 6 W/kg

Increase in heart schwannoma in male rats at highest dose – no increase in female rats, in male mice or in female mice
Indications of higher occurrences of tumours of brain and adrenal gland

National Toxicology Program Reports, 2018

Experimental exposure to animals not straightforward to be interpreted in terms of cumulative exposure in humans
**What is new – Human data?**

**Update of individual risk from comparing never mobile phone users with mobile phone users by number of years of use within UK Million Women Study**

**No association with ever use, daily use, 10+ years of use or specifically with tumours in the most exposed area of the brain (temporal and parietal)**

Not “new” in terms of data

Several reviews & meta-analyses

- Wang & Guo, J Cancer Res Therap, 2016
- Bortkiewicz et al., Int J Occup Med Env Health, 2017
- Prasad et al., Neurological Sci, 2017
- Yang et al., PLoS ONE, 2017
- Wang et al., World Neurosurg, 2018
- Röösli et al., Environ Int, 2019
- Choi et al., Int J Env Res Publ Health, 2020

**Overall confirmation of previous conclusions by the IARC and SCENIHR, as more or less based on same data**

Differences mainly due to how the risk of bias was interpreted

Meta-analyses unlikely to reveal new insights
### Mobile phone use in children, adolescents and young adults

<table>
<thead>
<tr>
<th>Cefalo</th>
<th>4 countries, ages 7-19 years</th>
<th>352 cases – 646 controls</th>
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<tbody>
<tr>
<td></td>
<td>1.0 (referent)</td>
<td></td>
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<tr>
<td>&gt; 3.3</td>
<td>1.35 (0.89 to 2.04)</td>
<td></td>
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<tr>
<td>3.3–5.0</td>
<td>1.47 (0.87 to 2.49)</td>
<td></td>
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<tr>
<td>&gt; 5.0</td>
<td>1.26 (0.70 to 2.28)</td>
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<table>
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<tr>
<th>Mobi-Kids</th>
<th>14 countries, ages 10-24 years</th>
<th>899 cases – 1,910 controls</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1.0 (referent)</td>
<td></td>
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<tr>
<td>≤ 35</td>
<td>1.33 (0.89 to 2.01)</td>
<td></td>
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<tr>
<td>36–144</td>
<td>1.44 (0.85 to 2.44)</td>
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<tr>
<td>&gt; 144</td>
<td>1.55 (0.86 to 2.82)</td>
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Aydin et al., J Natl Cancer Inst, 2011

Castano-Vinyals et al., Environ Int, 2022
**Population risk:**
- Incompatible with suggestions of increased glioma risk in ordinary mobile phone users
- Incompatible with suggestions of increased glioma risk in heavy mobile users other than heavy users of the first two generations
- Hypothetical small risks cannot be ruled out

**Glioma Incidence Rate (Nordic Countries)**

- **Men**
- **Women**

![Graph showing glioma incidence rate with observed and fitted values for different age groups (40-59, 20-39, 60-69, 70-84 years) with a trend line indicating increased incidence over years.]
Priority for re-evaluation of RF-EMF by IARC Monographs

• Advisory Group on Priorities (2020-2024) noted*
  • New evidence available for cancer bioassays and carcinogen mechanisms
  • Several likely informative cancer epidemiology studies forthcoming (Million Women Study ☑, Mobi-Kids ☑, COSMOS)

• Advisory Group recommended re-evaluation by IARC Monographs during 2023-24

• Any re-evaluation meeting would be announced 1 year in advance, at monographs.iarc.who.int

*https://monographs.iarc.who.int/advisory-group-to-recommend-priorities-for-the-iarc-monographs-during-2020-2024/
Conclusions

• Cancer Hazard: Possibility of carcinogenicity confirmed in large animal experiments Animal exposure not easy to interpret as cumulative lifetime human exposure

• Human risk from cohort and case-control studies: Possibility of modest risk for glioma in the <5% of heaviest mobile phone users Possibly only related to the first two generations of mobile technology Precaution: Possible risk can be mitigated by not holding the device directly to the head

• Population-level studies: No evidence of any detectable population risk of any type of brain tumour