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Source of funding and results of studies of health effects of mobile phone use: Systematic review of experimental studies

Anke Huss, PhD

ISPM, University of Bern, Switzerland

IRAS, University of Utrecht, The Netherlands

Institute for Risk Assessment Sciences



Why source of funding?

- biasing of studies can come from many sources
 - from very subtle influences in design and analysis
 - fraud at the other end of the spectrum
- Empirical studies have suggested that estimates of effect can be associated with funding source
 - Disclosure therefore informative
 - Assessment of more subtle influences hard to ascertain
- Reporting may be incomplete
 - expected as underreporting
 - depend on journal requirements



Background

- Use of mobile phones has increased considerably
- Part of the radiation is absorbed by the brain – raised concern
- Studies on the issue have produced controversial results
- Many of the studies were funded by industry – conflicts of interest?
 - Base station studies
 - Observational (Santini, Neila, ...)
 - Experimental (laboratory) studies
 - Mobile phone use studies
 - Observational (INTERPHONE)
 - Experimental
- Systematic literature review to assess effect of source of funding

Source of Funding and Results of Studies of Health Effects of Mobile Phone Use: Systematic Review of Experimental Studies

Anke Huss,¹ Matthias Egger,^{1,2} Kerstin Hug,³ Karin Huwiler-Müntener,¹ and Martin Röösli¹

¹Department of Social and Preventive Medicine, University of Berne, Berne, Switzerland; ²Department of Social Medicine, University of Bristol, United Kingdom; ³Institute of Social and Preventive Medicine, University of Basle, Basle, Switzerland

OBJECTIVES: There is concern regarding the possible health effects of cellular telephone use. We examined whether the source of funding of studies of the effects of low-level radiofrequency radiation is associated with the results of studies. We conducted a systematic review of studies of controlled exposure to radiofrequency radiation with health-related outcomes (electroencephalogram, cognitive or cardiovascular function, hormone levels, symptoms, and subjective well-being).

DATA SOURCES: We searched EMBASE, Medline, and a specialist database in February 2005 and scrutinized reference lists from relevant publications.

DATA EXTRACTION: Data on the source of funding, study design, methodologic quality, and other study characteristics were extracted. The primary outcome was the reporting of at least one statistically significant association between the exposure and a health-related outcome. Data were analyzed using logistic regression models.

data on the source of funding (industry, public or charity, mixed, not reported) and potential confounding factors, including study design (crossover, parallel, other), exposure (frequency band, duration, field intensity, and location of antenna), and methodologic and reporting quality. Four dimensions of quality were assessed (Jüni et al. 2001; Repacholi 1998): *a*) randomized, concealed allocation of study participants in parallel or crossover trials; *b*) blinding of participants and investigators to allocation group; *c*) reporting of the



Methods

- EMBASE/ PubMed Search in February 2005, reference lists, ELMAR (specialist database)
- Included:
 - Original studies, effect of controlled exposure of radiofrequency EMF from mobile phones on health-related outcomes (EEG, cognitive function, hormones, symptoms...), E/F/G language
 - Excluded studies of risk of mobile phone use when driving or EMF-incompatibilities



Primary outcome

- Reporting of at least one statistically significant outcome ($p < 0.05$) in the full text section
 - Crude measure (ignores size of effect)
 - unambiguous
 - Are sometimes interpreted as 'biological effect'



Further variables

- Design
- Funding, author affiliation, competing interests
- Sample size
- Exposure (frequency, sort & location of antenna, distance to head, exposure time, SAR value, time point of assessment (pre- /during/post exposure))
- Findings: No of findings/ no of stat. significant findings
- Main health outcome



Quality assessment

- Randomisation
- Blinding
- Statistics
- Exposure Assessment

For each item: adequate, inadequate, unclear

Identification of eligible studies

Potentially eligible articles identified (N=222)

Exclusions based on title or abstract (N=142)

- Studies of the risk of using mobile phones when driving a motor vehicle or operating machinery (N=29)
- Studies of the use of mobile phones in the monitoring of and communication with patients (N=28)
- Other study designs (N=29)
- Studies of interference with hearing aids or pacemakers (n=28)
- Studies of other exposures or methodological issues (N=26)
- Animal studies (N=2)

80 articles examined

Excluded (N=21)

- Other study design (N=9)
- Published in Chinese or Russian (N=3)
- Publication was withdrawn (N=1)
- Double publications (N=5)
- Studies of reducing exposure ("shielding studies") (N=2)
- Funded by company producing "shielding devices" (N=1)

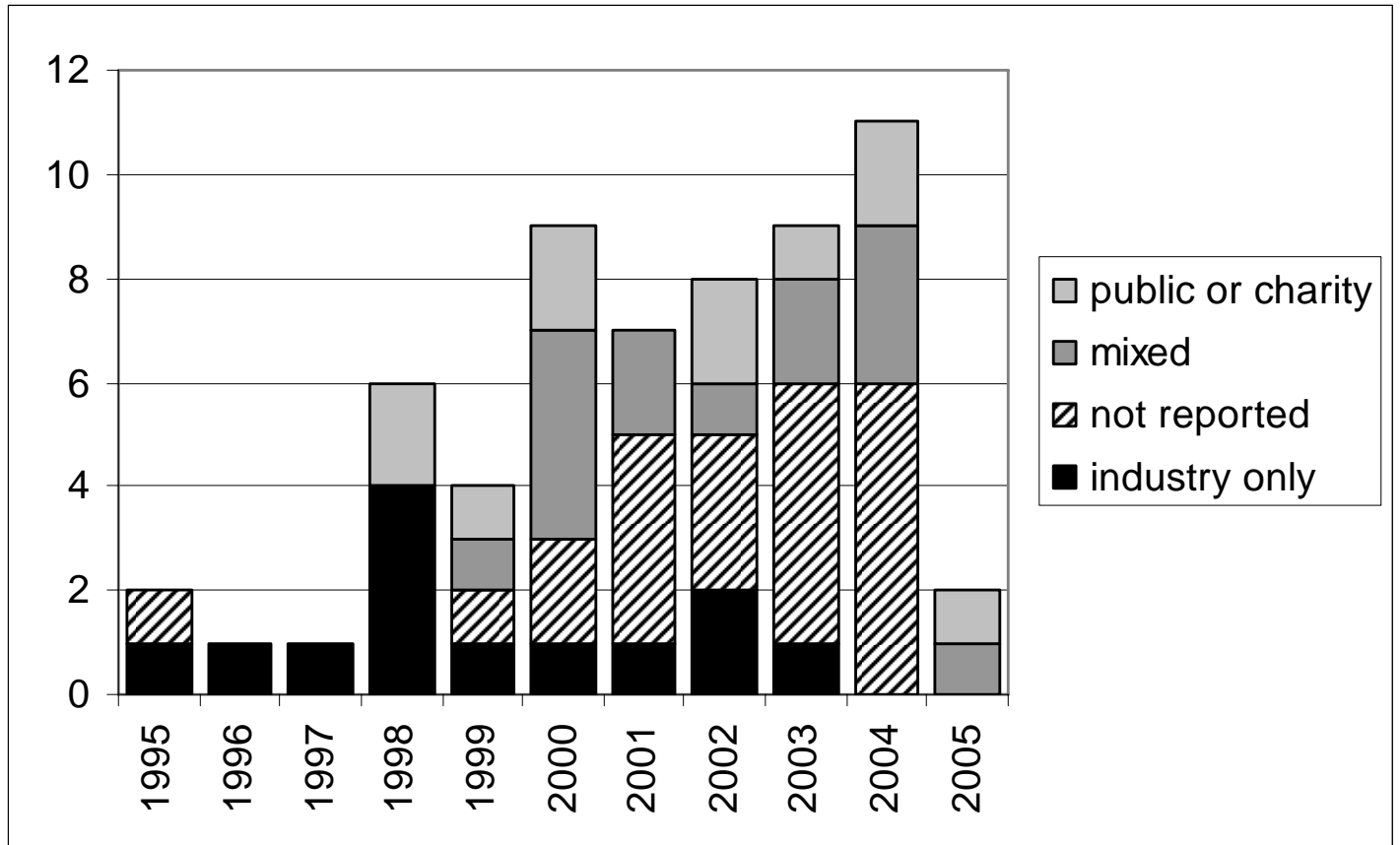
59 studies included in analyses



Results

- Main outcomes (>1 possible)
 - 54% EEG or brain physiology
 - 32% cognitive function
 - 12% hormones
 - 8% cardiovascular function
 - 5% symptoms
 - 18% other
- Design
 - 68% cross-over
 - 8% parallel
 - 24% other

Number of publications per year and their sources of funding





Results

- **Funding**

- Industry (N=12)
- public funding only (N=11)
- mixed (N=14)
- not reported (N=22)

- **Published statements of conflicts of interest**

- In none of the 31 journals (14 journals with IF > 1.5)
- 5 studies had authors with industry affiliation
- In 2005: 15 (48%) had a conflicts of interest policy

Quality

| | Source of funding | | | |
|-----------------------|-------------------|------------------|-----------------|---------------------------|
| | Indust. (n=12) | Public (n=11) | Mixed (n=14) | Not reported (n=22) |
| Study quality | | | | |
| Randomization | 10 (83.3%) | 7 (63.6%) | 13 (92.9%) | 9 (40.9%) |
| Blinding | 1 (8.3%) | 3 (27.3%) | 8 (57.1%) | 3 (13.6%) |
| Exposure (SAR) | 4 (33.3%) | 4 (36.4%) | 8 (57.1%) | 2 (9.1%) |
| Statistics | 3 (25%) | 3 (27.3%) | 7 (50%) | 1 (4.5%) |

Results

| | Source of funding | | | |
|---|-----------------------|------------------|-----------------------|---------------------------|
| | Industry (n=12) | Public (n=11) | Mixed (n=14) | Not reported (n=22) |
| Article text | | | | |
| Median number (range) of outcomes reported | 17.5 (4-31) | 10 (1-80) | 16 (9-44) | 7 (1-35) |
| Median number (range) of outcomes suggesting an effect at $p < 0.05$ | 0 (0 - 6) | 1.5 (0 - 7) | 3 (0 - 15) | 1.5 (0 - 12) |
| Odds ratio for reporting at least one result suggesting an effect ($p < 0.05$) | 0.11 (0.02 - 0.78) | 1 (ref.) | 0.56 (0.08 - 3.80) | 0.76 (0.12 - 4.70) |
| Odds ratio for reporting at least one result suggesting an effect ($p < 0.05$) <u>in abstract</u> | 0.29 (0.05 - 1.59) | 1 (ref.) | 1.43 (0.26 - 7.7) | 1.74 (0.35 - 8.42) |

Quality

| | Source of funding | | | |
|---|------------------------------|--------------------------------|------------------------------|------------------------------|
| | Industry (n=12) | Public or charity (n=11) | Mixed (n=14) | Not reported (n=22) |
| Crude | 0.11 (0.02 – 0.78) | 1 (ref.) | 0.56 (0.08 – 3.80) | 0.76 (0.12 – 4.70) |
| Adjusted for: | | | | |
| Type of study (crossover, parallel or other) | 0.08 (0.01 – 0.68) | 1 (ref.) | 0.38 (0.05 – 3.07) | 1.16 (0.16 – 8.61) |
| Randomization | 0.04 (0 - 0.56) | 1 (ref.) | 0.16 (0.01 - 2.15) | 1.27 (0.16 - 9.89) |
| Blinding | 0.14 (0.02 - 0.96) | 1 (ref.) | 0.54 (0.08 - 3.91) | 0.76 (0.12 - 4.8) |
| Statistics | 0.12 (0.02 - 0.85) | 1 (ref.) | 0.67 (0.09 - 4.85) | 0.54 (0.08 - 3.76) |
| Exposure | 0.13 (0.02 - 0.89) | 1 (ref.) | 0.47 (0.07 - 3.39) | 0.86 (0.14 - 5.5) |

Exposure

| | Source of funding | | | |
|------------------------------------|-------------------------|--------------------------------|-----------------------|---------------------------|
| | Industry (n=12) | Public or charity (n=11) | Mixed (n=14) | Not reported (n=22) |
| Crude | 0.11 (0.02 – 0.78) | 1 (ref.) | 0.56 (0.08 – 3.80) | 0.76 (0.12 – 4.70) |
| Adjusted for: | | | | |
| Position of antenna next to ear | 0.08 (0.01 – 0.65) | 1 (ref.) | 0.57 (0.08 – 3.97) | 0.71 (0.11 – 4.48) |
| Use of 900 MHz band | 0.12 (0.02 – 0.8) | 1 (ref.) | 0.58 (0.08 – 4.03) | 0.74 (0.12 – 4.65) |
| Duration | 0.045 (0.003 - 0.69) | 1 (ref.) | 0.26 (0.024 - 2.9) | 0.48 (.045 - 5.04) |

Health Outcome

| | Source of funding | | | |
|---------------------------------|------------------------------|--------------------|------------------------------|------------------------------|
| | Industry (n=12) | Public (n=11) | Mixed (n=14) | Not reported (n=22) |
| Crude | 0.11 (0.02 – 0.78) | 1 (ref.) | 0.56 (0.08 – 3.80) | 0.76 (0.12 – 4.70) |
| Adjusted for: | | | | |
| Electroencephalogram | 0.09 (0.01 - 0.67) | 1 (ref.) | 0.48 (0.07 - 3.46) | 0.68 (0.11 - 4.42) |
| Cognitive function tests | 0.14 (0.02 - 0.98) | 1 (ref.) | 0.42 (0.06 - 3.11) | 0.7 (0.11 - 4.44) |
| Hormone levels | 0.11 (0.02 - 0.82) | 1 (ref.) | 0.48 (0.07 - 3.43) | 0.75 (0.12 - 4.79) |
| Cardiovascular function | 0.12 (0.01 - 0.99) | 1 (ref.) | 0.56 (0.08 - 3.8) | 0.77 (0.12 - 4.85) |
| Wellbeing or symptoms | 0.11 (0.02 - 0.78) | 1 (ref.) | 0.56 (0.08 - 3.82) | 0.77 (0.12 - 4.87) |
| Other | 0.11 (0.02 - 0.78) | 1 (ref.) | 0.57 (0.08 - 3.98) | 0.77 (0.12 - 4.83) |



Summary

- Studies exclusively funded by industry are less likely to report statistically significant effects
- Conflicts of interest should be published
- Interpretation of results: take sponsorship into account



What has happened since 2005?

- Embase, ELMAR, EMF-Portal search (Oct 2009)
- 75 additional experimental studies (mob phone)
 - checked source of funding
 - conflicts of interest
 - author affiliation
 - health endpoint reported in abstract
 - any significant result reported in abstract

Results

| | Industry | Public | Mixed | Not reported | Total |
|--|---------------------|---------------------|---------------------|---------------------|-----------------------|
| Systematic review until Feb. 2005 | 12 (20%) | 11 (19%) | 14 (24%) | 22 (37%) | 59 (100%) |
| Feb. 2005 – Oct 2009 | 11 (15%) | 12 (16%) | 33 (44%) | 19 (25%) | 75 (100%) |
| Total | 23 (17%) | 26 (19%) | 44 (33%) | 41 (31%) | 135 (100%) |



Results

| Outcomes | 1995-2005 | 2005-2009 |
|--------------------|------------------|------------------|
| EEG | 54% | 38/75 (51%) |
| cognitive outcomes | 32% | 24/75 (32%) |
| hormones | 12% | 3/75 (4%) |
| cardiovascular | 8% | 15/75 (20%) |
| well-being | 5% | 10/75 (13%) |

Results

| | Source of funding | | | |
|---|-----------------------|-------------|-----------------------|------------------------|
| | Industry | Publ. | Mixed | Not reported |
| 1) Odds ratio for reporting at least one result suggesting an effect ($p < 0.05$) <u>in abstract</u> | 0.29 (0.05 - 1.59) | 1 (ref.) | 1.43 (0.26 - 7.7) | 1.74 (0.35 - 8.42) |
| 2a) Odds ratio for reporting at least one result suggesting an effect ($p < 0.05$) <u>in abstract</u> | 1.00 (0.22 - 4.63) | 1 (ref.) | 1.33 (0.42 - 5.54) | 3.67 (1.12 - 12.05) |
| <u>Excl. studies with firewall</u> | | | | |
| 2b) Odds ratio for reporting at least one result suggesting an effect ($p < 0.05$) <u>in abstract</u> | 0.33 (0.04 - 3.06) | 1 (ref.) | 1.33 (0.42 - 5.54) | 3.67 (1.12 - 12.05) |



Results - CoI

- 8 (11%) publications reported a conflicts of interest statement
 - all reported no conflicts:
 - 1 industry, 2 mixed, 4 public, 1 not reported
- 7 publications with authors with industry affiliation:
 - none reported on potential conflicts of interest
- 2 publications with industry funding reported they had implemented a firewall



Summary

- first review source of funding explained some of the heterogeneity of results
- disclosure statements should be published
- however, these are rarely reported – also in more recent publications
- this included also journals with disclosure policy
- disclosure and our own biases - fair assessment necessary



Outlook

- International Committee of Medical Journal Editors - ICMJE
- published a uniform format for disclosure information
 - quite comprehensive
 - goal is to ensure transparency
 - usefulness has yet to be shown



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