

References

- ¹ Sanghavi P. Commentary: culpability analysis won't help us understand crash risk due to cell phones. *Int J Epidemiol* 2013;**42**:267–69.
- ² Asbridge M, Brubacher JR, Chan H. Cell phone use and traffic crash risk: a culpability analysis. *Int J Epidemiol* 2013;**42**:259–67.
- ³ Brubacher J, Chan H, Asbridge M. Letter. Culpability analysis is still a valuable technique. *Int J Epidemiol* 2014;**43**:270–2.

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The case of acoustic neuroma: Comment on: Mobile phone use and risk of brain neoplasms and other cancers

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Benson *et al.* recently published in this journal analyses of the Million Women Study to study tumour incidence in relation to the use of mobile phones¹. Based on their analyses of this exceptionally large and valuable cohort, the authors concluded that their study did not show any increased incidence of glioma, meningioma or non-CNS cancers. However, it is surprising that the important positive finding of their study showing a statistically significant increased risk of acoustic neuroma [relative risk (RR) 2.46, 95% confidence interval (CI) 1.07–5.64] with long-term (10+) use of mobile phones was not included in the conclusion section of the abstract and was only discussed after pooling with the Danish prospective cohort in the conclusion section of the paper.

This is surprising given that the finding provides further support for the Working Group of the IARC monograph programme conclusion to classify radio frequency electromagnetic fields as 'possibly carcinogenic to humans' (Group 2B) based on limited evidence from epidemiological studies for acoustic neuroma (and glioma, but not meningioma).² The finding itself is further strengthened by an observed clear dose-response association; with RR = 1.00 (0.54–1.82) for <5 years of use, RR = 1.80 (1.08–3.03) for 5–9 years of use and finally RR = 2.46 for 10+ years of use.

The main argument for not interpreting these results as indicative of a causal association between long-term mobile phone use and increased risk of acoustic neuroma, even in the presence of a clear dose-response associations, is that after pooling the data from this study with those of the Danish prospective study,³ the pooled risk estimate is non-statistically significant with a RR of 1.16 [95% CI 0.75–1.81] for mobile phones use for at least 10 years. As outlined by the authors, the rationale for *post hoc* pooling of two studies from different populations was that both

were prospective cohort studies that did not suffer from the recall bias in case-control studies: most notably the INTERPHONE study⁴ and work published by Hardell *et al.*⁵ However, the Danish prospective cohort study³ is also not free from bias,^{6–9} most notably because of problems with correct identification of mobile phone subscribers between 1987 and 1995 (with all non-participants (42%), including business users, classified as 'non-exposed'). These problems in the design of the Danish study will have biased any risk estimates towards the null,¹⁰ and pooling therefore has inevitably led to a reduction in the effect size; despite the strengths of the Million Women Study in itself. A common and more transparent approach would have been to conduct a meta-analysis of all available scientific papers (incorporating each study with its own strengths and weaknesses), instead of *post hoc* and selective pooling of data as done by Benson *et al.*¹

The epidemiological evidence on long-term (10+ years) use of mobile phones and risk of acoustic neuroma is summarized in Table 1, with the results of the random-effects meta-analysis also shown graphically in Figure 1. As shown, the accumulated scientific evidence remains inconclusive, but does indicate a 14–43% summary increased risk of acoustic neuroma because of long-term (10+ years) use of mobile phones, although without reaching statistical significance (95% CI 0.76–2.67).

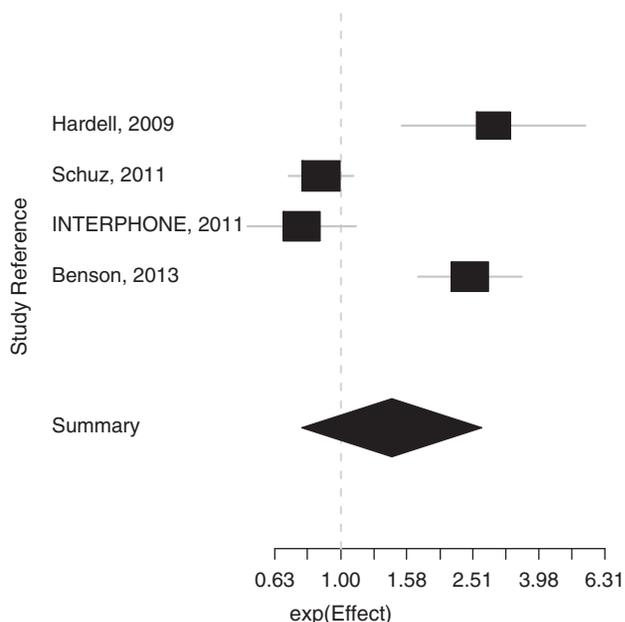
In conclusion, in contrast to conclusions on acoustic neuroma by Benson *et al.*¹ a meta-analytic approach indicates, in agreement with the conclusions from the IARC monograph programme,³ that long-term (10+ years) mobile phone use may lead to increased risk but, not surprisingly, that the evidence is not yet conclusive. Future prospective studies with improved exposure assessment using records of mobile phone

Table 1 Overview of studies on long-term use of mobile phones and acoustic neuroma and results of meta-analysis

Study identifier	Design	Time since first use (years)	RR	95% OR
Benson 2013 ¹	Cohort	10+	2.46	1.72–3.53
Schuz 2011 ³	Cohort	11+	0.87	0.69–1.09
INTERPHONE 2011 ^{4,a}	Case-control	10+	0.76	0.52–1.11
Hardell 2009 ^{5,b}	Case-control	11+	2.90	1.6–5.5
Meta-analytic summary	Fixed-effects		1.14	0.97–1.35
	Random-effects		1.43	0.76–2.67

^aAlthough many of the INTERPHONE country-specific results have also been separately published, the pooled summary estimate has been used here.

^bPooled estimate of two case-control studies by the same group using identical questionnaires.

**Figure 1** Forest plot random-effects meta-analysis

use, most notably the COSMOS study,¹¹ will hopefully sway the cumulative results of the meta-analysis in a conclusive direction and settle this debate.

References

- Benson VS, Pirie K, Schüz J *et al.* Mobile phone and risk of brain neoplasms and other cancers: prospective study. *Int J Epidemiol* 2013;**42**:792–802.

- Baan R, Grosse Y, Lauby-Secretan B *et al.* Carcinogenicity of radio frequency electromagnetic fields. *Lancet Oncol* 2011;**12**:624–26.

- Schüz J, Steding-Jessen M, Søren H *et al.* Long-term mobile phone use and the risk of vestibular schwannoma: a Danish nationwide cohort study. *Am J Epidemiol* 2011;**174**:416–22.

- INTERPHONE. Acoustic neuroma risk in relation to mobile telephone use: Results of the INTERPHONE international case-control study. *Cancer Epidemiol* 2011;**35**:453–64.

- Hardell L, Carlberg M. Mobile phones, cordless phones and the risk of brain tumours. *Int J Oncology* 2009;**35**:5–17.

- Ahlbom A, Feychting M, Cardis E, Elliott P. Re: Cellular telephone use and cancer risk: update of a nationwide Danish cohort study. *J Natl Cancer Inst* 2007;**99**:655.

- Kundi M. Failure to detect a link between mobile phone use and brain tumours in a large Danish cohort study: but findings may be due to bias. *Evid Based Med* 2012;**17**:165–66.

- Philips A, Lamburn G. Updated study contains poor science and should be disregarded. *BMJ* 2011;**343**:d7899.

- Khurana VG. Questions about selection, exposure, and tumour incidence. *BMJ* 2011;**343**:d7893.

- Söderqvist F, Carlberg M, Hardell L. Review of four publications on the Danish cohort study on mobile phone subscribers and risk of brain tumours. *Rev Environ Health* 2012;**27**:51–58.

- Schüz J, Elliott P, Auvinen A *et al.* An international prospective cohort study of mobile phone users and health (COSMOS): design considerations and enrolment. *Cancer Epidemiol* 2011;**35**:37–43.

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