Mobile phones and risk of cancer - what has epidemiology found?

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Mobile phone studies

- Focus has been on tumors in the head and neck region
- Mostly brain tumors
  → Glioma, meningioma, acoustic neuroma
- A few studies on parotid gland tumors
- Single studies on uveal melanoma, lymphoma, other tumors

Brain tumors

- Around 15 studies available on brain tumors and mobile phone use

- Four groups of studies:
  - → Early US-studies
    - Short duration of use
  - → Nordic registry based studies (subscriber data)
  - → Hardell et al.: 3 studies from Sweden
  - → Interphone studies: international collaborative studies performed in 13 countries with a common protocol

Glioma and mobile phone use, **short** induction period

Study	Exp cases	RR (95 % CI)	Comments
Muscat 2000	28	1.1 (0.6-2.0)	2-3 yrs, Glioma
Inskip 2001	51	1.0 (0.6-1.6)	0.5-3 yrs, Glioma
Johansen 2001, cohort	87	1.1 (0.9-1.3)	1-4 yrs; Brain, nervous system
Schüz 2006, cohort	266	1.0 (0.9-1.2)	1-4 yrs; Brain, nervous system
Auvinen 2002	15+11	1.2 (0.7-2.0)	1-2 yrs, Glioma
Hardell 1999	78	1.0 (0.7-1.4)	>1 years, brain tumors
Hardell 2002	79	1.1 (0.8-1.6)	> 1 yr; Analogue, Malignant
	112	1.1 (0.9-1.5)	> 1 yr; Digital, Malignant
Hardell 2005	100	**1.6 (1.1-2.4)**	1-5 yrs; Digital, Malignant
Lönn 2005	112	0.8 (0.6-1.1)	1-4 yrs; Glioma
Christensen 2005	43	0.7 (0.3-1.0)	1-4 yrs; Glioma
Hepworth 2006	271	0.9 (0.7-1.1)	1-4 yrs; Glioma
Schüz 2006	82	0.9 (0.6-1.2)	1-4 yrs; Glioma
Lahkola 2007	504	0.8 (0.6-0.9)	0.5-4 yrs; Glioma
Hours 2007	13	1.0 (0.4-2.5)	16-27 months, Glioma
Takebayashi 2008	11	0.9 (0.4-2.3)	<2.2 yrs; Glioma

Glioma, short induction period

Up to 5 years of use:

- Considerable amount of data available, most studies have large numbers
- Very consistent results: no indication of increased risk within 5 years of use

  → Only one study differs, Hardell 2005

- Pooled risk estimate: 0.92 (95% CI 0.86-0.99)

Glioma, short induction period

5 to 10 years of use:

- Large amount of data available
- Very consistent results in larger studies, data do not indicate increased risk within 10 years of use

  → Only one study differs, Hardell 2005
- Pooled risk estimate: 0.97 (95% CI 0.89-1.05), heterogeneity between studies
- Pooling without Hardell 2005: 0.92 (95% CI 0.85-1.01), no heterogeneity

Brain tumors and mobile phone use, **long** induction period

	Exp cases	**RR (95 % CI)**	**Comments**
Schüz 2006, cohort study	28	0.66 (0.44-0.95)	≥10 yrs; Brain, nervous system
Hardell 1999	16	1.2 (0.6-2.6)	>10 years, brain tumors
Hardell 2002	43 12	1.2 (0.8-1.8) 1.7 (0.7-4.3)	> 6 years; Analogue, Malignant > 6 years; Digital, Malignant
Hardell 2005	48 19	3.5 (2.0-6.4) 3.6 (1.7-7.5)	>10 years; Analouge, Malignant >10 years; Digital, Malignant
Lönn 2005	25	0.9 (0.5-1.5)	≥10 years; Glioma
Christensen 2005	14	0.7 (0.3-1.6)	≥10 years; Glioma
Hepworth 2006	66	0.9 (0.6-1.3)	≥10 years; Glioma
Schüz 2006	12	2.2 (0.9-5.1)	≥10 years; Glioma
Lahkola 2007	143	0.95 (0.73-1.23)	≥10 years; Glioma
Takebayashi 2008	7	0.6 (0.2-1.8)	≥6.5 years; Glioma

Glioma, long induction period

More than 10 years of use:

- Less data available, although Interphone provides large numbers (about 70% are published)
- Smaller studies leads to more variability in results
- Largest studies show risk estimates close to one
  → Except study by Hardell 2005
- Pooled risk estimate: 1.08 (95% CI 0.93-1.26)
  → Heterogeneity between studies!
- Pooling without Hardell 2005: 0.95 (95% CI 0.81-1.11)
  → No heterogeneity

Nordic and UK Interphone studies combined

Lahkola et al. Int J Cancer 2007,

Case-control study: 1521 glioma cases and 3301 controls

Mobile phone use

Years since start	**OR (95% CI)**	**No. exp. cases**
0.5-4	0.77 (0.65-0.92)	384
5-9	0.75 (0.62-0.90)	342
≥10	0.95 (0.74-1.23)	143
Side of head:	*Same*	*Opposite*
0.5-4	1.08 (0.88-1.31)	0.70 (0.57-0.87)
5-9	1.10 (0.89-1.35)	0.74 (0.59-0.92)
≥10	1.39 (1.01-1.92)	0.98 (0.71-1.37)

Risk estimates in relation to side of use

	Ipsilateral*	Contralateral*	Overall
Hardell 1999/2001	1.1 (0.6-1.8)	0.7 (0.4-1.2)	1.0
Hardell 2002	1.9 (1.2-3.0)	0.6 (0.4-1.1)	1.1
Lönn 2005	1.1 (0.7-1.4)	0.7 (0.5-1.1)	0.8
Hardell 2005	3.1 (1.6-6.2)	2.6 (1.3-5.4)	2.6
Hepworth 2006	1.2 (1.0-1.5)	0.8 (0.6-0.9)	0.9

No overall effect, but increased risk for ipsilateral use and protective effects for contralateral use: Recall bias when reporting side of use likely explanation

* Ipsilateral = tumor and mobile phone use on the same side of the head
Contralateral = tumor and mobile phone use on opposite sides of the head

Brain tumors and mobile phone use - conclusions

- Taken together, evidence support that short term mobile phone use (<10 years) **do not** affect risk
- For long term mobile phone use, ≥10 years, most data speak against an increased risk
  - → Some uncertainty regarding ipsilateral use – recall bias is likely to affect findings
- No data available for use more than 15 – 20 years
  - → Mobile phones are still relatively new
- No data available on children

Acoustic neuroma

- Benign tumor that arises on the eighth cranial nerve leading from the brain to the inner ear
- Early symptoms:
  - → Unilateral (one-sided) hearing loss
  - → Tinnitus
  - → Dizziness/loss of balance
- Grows slowly during a period of years before being diagnosed, about half of tumors do not grow further after detection
- Needs to be removed if it pressures on surrounding tissue
- Average time between first symptoms and diagnosis >5 years (Thomsen J, 1990)

Acoustic neuroma and mobile phone use

	Exp cases	RR (95 % CI)	Comments
Inskip 2001	22	1.0 (0.5-1.9)	Regular use
Muscat 2000	7	0.8 (0.4-1.7)	> 1 year
Johansen 2001, cohort	7	0.6 (0.3-1.3)	Ever mobile phone subscription
Schüz 2006, cohort	32	0.73 (0.50-1.03)	Ever mobile phone subscription
Hardell 1999	13	0.8 (0.1-4.2)	>1 year
Hardell 2002	38 23	3.5 (1.8-6.8) 1.2 (0.7-2.2)	>1 year, analogue >1 year, digital
Hardell 2005	20 53	4.2 (1.8-10) 2.0 (1.05-3.8)	>1 year, analogue >1 year, digital
Christensen 2005	45	0.9 (0.5-1.6)	Regular use
Lönn 2005	89	1.0 (0.6-1.5)	>1 year regular use
Schoemaker 2005	360	0.9 (0.7-1.1)	>1 year regular use
Schlehofer 2006	29	0.7 (0.4-1.2)	>1 year regular use
Takebayashi 2007	51	0.7 (0.4-1.2)	>1 year regular use

Hardell studies, acoustic neuroma

	Exp cases	RR (95 % CI)	Years since first use
Hardell 2002	12	3.0 (1.0-9.3)	1-5 yrs; Analogue
	19	3.8 (1.4-10.2)	>5-10 yrs; Analogue
	7	3.5 (0.7-16.8)	>10 yrs; Analogue
Hardell 2005	2	9.9 (1.4-69)	1-5 yrs; Analogue
	11	5.1 (1.9-14)	>5-10 yrs; Analogue
	7	2.6 (0.9-8.0)	>10 yrs; Analogue
	29	1.7 (0.9-3.5)	1-5 yrs; Digital
	23	2.7 (1.3-5.7)	>5-10 yrs; Digital

Results from larger Interphone studies

	No. exp cases	RR (95 % CI)	Time since first use
Lönn 2004	44 30 14	0.8 (0.5-1.3) 1.1 (0.6-1.8) 1.9 (0.9-4.1)	1-4 yrs 5-9 ≥ 10
Schoemaker 2005	231 96 31	0.8 (0.7-1.0) 0.9 (0.7-1.2) 1.0 (0.7-1.5)	0.5-4 yrs 5-9 ≥ 10

Acoustic neuroma - laterality

	Ipsilateral*	Contralateral	Time since first use
Lönn 2004	3.9 (1.6-9.5)	0.8 (0.2-2.9)	≥ 10 years
Schoemaker 2005	1.3 (0.8-2.0) 1.8 (1.1-3.1)	1.0 (0.6-1.7) 0.9 (0.5-1.8)	≥ 10 years Duration of use ≥10 years
Hardell 2005	5.1 (1.9-1.4)	4.9 (1.2-21)	Analogue >1 year

* Ipsilateral = tumor and mobile phone use on the same side of the head

Potential bias in studies of acoustic neuroma

- Likely that tumor side affect cases' report of side of mobile phone use
  - → Cases may tend to overreport use on the same side
  - → Cases who used the phone on the same side have changed side after the occurrence of the disease (hearing loss)

- Possible that exposure may influence detection of tumor
  - → Unilateral hearing loss discovered during mobile phone use

Acoustic neuroma - conclusions

- Taken together, evidence support that short term mobile phone use (<10 years) **do not** affect risk
- For long term mobile phone use, the possibility of an increased risk cannot be excluded, additional data are needed
  - → Number of long term users are small in most studies
  - → Recall bias is a problem

Future research

- Additional research is needed to evaluate long term use – improved exposure assessment is essential
  - → Need to address problems with recall bias and non-differental exposure misclassification
- Cohort study with prospectively collected information on amount of mobile phone use, both self-reported and operator data – COSMOS study ongoing
  - → Will minimize exposure misclassification
  - → No risk of recall bias
- Studies on brain tumors in children underway
  - → Cefalo study will report results early 2010