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2. CANCER IN HUMANS

This section is a review of the large body of epidemiological evidence from studies of exposure of occupational groups and the general population to radiofrequency (RF) radiation from diverse sources, including from the use of mobile telephones. The results of these studies comprise a large amount of data, which could not be fully reproduced here. The Working Group included studies that assessed specific sources of RF radiation or job titles that were specifically linked to RF radiation. Studies that were excluded used job titles only for classification, or source surrogates only, without specifically addressing RF exposure. The Tables in this section summarize the main findings, but do not uniformly capture the results for all exposure metrics or all subgroups given in the original publications. In the text, the Working Group provides comments on those findings that are of greatest relevance to the evaluation, e.g. risk in the overall exposed group, patterns of change in risk with increasing exposure (such as a monotonic increase in risk with increasing exposure), and changes in risk with duration of exposure or latency.

2.1 Occupational exposure

The occupational environment is one domain in which humans are exposed to RF radiation. Many occupational circumstances entail regular or occasional exposure to RF radiation from fixed or mobile sources. A wide variety of workers are involved, including military and security personnel using walkie-talkie devices, radar operators, radio and television antenna maintenance and repair workers, welders performing dielectric (high-frequency) welding and sealing of plastics, workers using RF radiation for drying or testing operations, and physiotherapists employing medical diathermy equipment. Only a limited number of studies have assessed the risk of cancer in relation to either measured or inferred levels of exposure. There have been a large number of epidemiological studies of workers who were not evaluated in terms of their exposure to RF radiation, but rather with respect to their exposure to electric or magnetic fields (EMF), extremely low-frequency (ELF) fields, i.e. < 300Hz (IARC, 2002), or microwaves (MW), and an even larger number of studies in which it might be suspected that some workers were likely to have been exposed to RF radiation. The Working Group did not include these studies in the present review because it was not certain that sizable fractions of the workers in such studies were actually exposed to RF radiation, or at what levels they were exposed. This review is therefore limited to occupational studies in which the investigators made an effort to specifically document or assess exposures to RF radiation in the workers considered to be exposed.

2.1.1 Cancer of the brain

(a) Case–control studies

Thomas *et al.* (1987) conducted a death-certificate-based case–control study in selected counties of the north-eastern and southern United States of America (USA). The cases were men who had died from tumours of the brain or other parts of the central nervous system (CNS) at age ≥ 30 years between 1978 and 1981. Diagnoses were verified in hospital records. One control decedent, whose cause of death was not brain cancer, epilepsy, stroke, suicide or homicide, was selected for each case, and matched by age and year of death, and usual area of residence. The next-of-kin of the study subjects were interviewed: participation rates were 74% for cases and 63% for controls. For each job held since age 15 years, the job title and a brief description of the work, the industry, the location, the employment dates, and the hours worked per week were obtained. Two methods were used to classify men according to their occupational exposure to MW or RF radiation: one was based on a selection of broad job titles [most of which would have had mixed or predominant exposure to EMF frequencies other than RF], while in the other an industrial hygienist classified each job according to exposure to RF radiation, lead and soldering fumes. Data from 435 cases and 386 controls were analysed. Only results based on the industrial hygienist's classification are reviewed here. [While controls were individually matched to cases, there was a deficit of controls, possibly due to poorer participation, but no mention was made of adjusting for the matching variables in the analysis; thus there may have been uncorrected bias due to study design in the calculated odds ratios (ORs).] Risk of brain tumours was increased in those ever occupationally exposed to RF radiation (OR, 1.7; 95% CI, 1.1–2.7) adjusted for educational level (Table 2.1); however, the odds ratio decreased when men also exposed to soldering fumes or lead were removed from the exposed group, and dropped even further when those who might also have had exposure to organic solvents were removed from the exposed group. [This study was one of the few to directly attempt to address possible confounding of occupational exposure to RF radiation with coexposure to soldering fumes, lead and organic solvents. It was limited by the fact that it was based on death certificates (the dead controls were unlikely to accurately represent the population from which the dead cases came) and on an analysis that may not have controlled for bias due to the matched design.]

Berg *et al.* (2006) analysed data obtained from cases (glioma and meningioma) and controls using a detailed questionnaire on occupational exposure to what the authors described as RF/MW/EMF, which formed part of the data collected in the German component of the INTERPHONE study (as described in Section 2.2.2 in relation to Schüz *et al.*, 2006a). Participants were asked screening questions about use of industrial heating equipment to process food, to bond, seal, and weld materials, or to melt, dry, and cure materials. Questions were also asked about manufacturing semiconductor chips or microelectronic devices; using radar; maintaining electromagnetic devices used to treat or diagnose diseases; working with or nearby to broadcasting and telecommunications antennae and masts; using different kinds of transmitters; and using amateur ("ham") radio. When a participant screened positive for one of these activities, further questions were asked to determine whether the occupation entailed exposure to RF/MW/EMF. Each person was classified as having: no exposure (responded negatively to the screening questions, or were positive for some activities thought not to entail exposure); no probable exposure (exposure existed but probably not exposed continuously during working hours in any activity); probable exposure (probably exposed continuously during working hours in at least one activity); or high exposure

Table 2.1 Case–control studies on cancer of the brain and occupational exposure to radiofrequency radiation

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Comments
Thomas *et al.* (1987) USA, 1979–81	435	386	Death certificates of residents who had died from a cause other than brain tumour, epilepsy, stroke, suicide or homicide, matched to cases by age and year at death, and area of residence	Next-of-kin interviews regarding employment history and other risk factors for brain tumours. Exposure classified according to job title and results of previous studies, and by an industrial hygienist	Brain	*Occupational exposure to MW or RF based on assessment by the industrial hygienist*			Restricted to white men aged > 30 yr. Methods of statistical analysis were not described. Covariates: matched by age and year at death, and area of residence, but not included as covariates in the unmatched analysis
						Never exposed		1.0	
						Ever exposed		1.7 (1.1–2.7)	
						Ever exposed, excluding those with co-exposure to soldering fumes or lead		1.4 (0.7–3.1)	
						Ever exposed, excluding those with co-exposure to organic solvents	2	0.4 (NR)	

Table 2.1 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Comments
Berg *et al.* (2006) Germany, 2000–03	381 cases of meningioma, 366 cases of glioma	1494, of whom 732 matched to glioma and 762 to meningioma cases	2449 controls frequency-matched on age, sex and centre, were derived from population registries, 63% participated. Subsequently, controls were matched to cases on a 2:1 basis	CAPI mostly in hospital for cases, and at home for controls. Interview included questions about job title and specific occupational activities followed by expert assessment of exposure to RF/MW	Glioma (C71.0–71.9; 9380–9383, 9390–9393, 9400–9401, 9410–9411, 9420–9421, 9440–9442, 9450–9451) and meningioma (C70.0; 9530–9539)	*Exposure to RF* *Glioma* Total exposure: No/not probable Probable/high exposure Probable exposure: No exposure Not probable Probable High Duration of high exposure: Not highly exposed Highly exposed for < 10 yr Highly exposed for ≥ 10 yr	 328 38 308 20 16 22 344 9 13	 1.00 1.04 (0.68–1.61) 1.00 0.84 (0.48–1.46) 0.84 (1.46–1.56) 1.22 (0.69–2.15) 1.00 1.11 (0.48–2.56) 1.39 (0.67–2.88)	Aged 30–69 yr Covariates: SES, urban or rural, exposure to ionizing radiation, smoking history, age at diagnosis

Table 2.1 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Comments
Berg *et al.* (2006) (contd.)						*Meningioma*			
						Total exposure:			
						No/not probable	355	1.00	
						Probable/high exposure	26	1.12 (0.66–1.87)	
						Probable exposure:			
						No exposure	340	1.00	
						Not probable	15	1.11 (0.57–2.15)	
						Probable	15	1.01 (0.52–1.93)	
						High	11	1.34 (0.61–2.96)	
						Duration of high exposure:			
						Not highly exposed	370	1.00	
						Highly exposed for < 10 yr	5	1.14 (0.37–3.48)	
						Highly exposed for ≥ 10 yr	6	1.55 (0.52–4.62)	

Table 2.1 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Comments
Karipidis *et al.* (2007) Australia, 1987–91	416	422	Population of four major centres as recorded by the electoral rolls for the Australian state of Victoria	Comprehensive job history, including self-reported RF exposure in each job, expert assessment by occupational hygienist and application of a community-based job-exposure matrix, FINJEM	Glioma (ICD-O codes 938–946)	*Total cumulative exposure to RF given by FINJEM ($W/m^2.yr$)*			Covariates: age, sex, and year of education
						Unexposed	396	1.00	
						> 0–11	4	0.57 (0.16–1.96)	
						> 11–52	8	1.80 (0.53–6.13)	
						> 52	6	0.89 (0.28–2.81)	
						P trend		0.91	
						Self-reported duration of exposure (yr) to RF			
						Unexposed	385	1.00	
						> 0–3	9	0.53 (0.23–1.21)	
						> 3–8	8	0.43 (0.18–1.00)	
						> 8	12	0.82 (0.37–1.82)	
						P trend		0.08	
						Expert assessment of duration of exposure (yr) to RF			
						Unexposed	381	1.00	
						> 0–3	10	1.20 (0.48–3.04)	
						> 3–6	12	1.65 (0.66–4.17)	
						> 6	11	1.57 (0.62–4.02)	
						P trend		0.17	

Table 2.1 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Comments
Baldi *et al.* (2011) France, 1999–2001	221	442	Population selected from local electoral rolls and individually matched on age, sex and department of residence	Interviewer-administered face-to-face questionnaire, which included a lifetime occupational history documenting for each job held for ≥ 6 mo: job title, industry, begin and end dates, and details of tasks performed. Occupational hygienists assessed probability of exposure to RF and duration for each job.	CNS (70.0–70.9, 71.0–71.9, 72.2–72.9)	*Occupational exposure to RF* All brain tumours (n = 221): Unexposed Exposed Glioma (n = 105): Unexposed Exposed Meningioma (n = 67): Unexposed Exposed Acoustic neurinoma (n = 32): Unexposed Exposed *Amateur radio practice* All brain tumours (n = 221): No Yes	 148 7 71 7 61 0 31 1 NR NR	 1.00 1.50 (0.48–4.70) 1.00 1.44 (0.50–4.13) 1.00 - 1.00 0.40 (0.05–3.42) 1.00 1.39 (0.67–2.86)	95 males, 126 females. 70% of eligible cases participated and 69% of eligible and contactable controls. Covariates: exposure to pesticides, smoking, educational level

CAPI, computer-assisted personal interview; FINJEM, FIN(nish) job-exposure matrix; mo, month; MW, microwave; NR, not reported; RF, radiofrequency radiation; SES, socioeconomic status; W, watt; yr, year

(certainly exposed continuously during working hours and sometimes at levels > 0.08W/kg in at least one activity). Analyses included data from proxy interviews, and results were not sensitive to removal of proxy interview data. There was weak evidence that risk of glioma and of meningioma increased with increasing duration of high occupational exposure to RF/MW/EMF. For glioma, the odds ratio for < 10 years of high exposure relative to no exposure was 1.11 (95% CI, 0.48–2.56) and that for ≥ 10 years of high exposure was 1.39 (95% CI, 0.67–2.88); the analysis controlled for centre, sex, age at diagnosis, socioeconomic status, urban or rural area, exposure to ionizing radiation, and smoking history. The corresponding odds ratios for meningioma were 1.14 (95% CI, 0.37–3.48) and 1.55 (95% CI, 0.52–4.62) (Table 2.1). [The strengths of this study were its large size and evaluation of exposure at the job-activity level. Its main weaknesses included the small numbers of cases with high exposure and lack of associated consideration of other sources of exposure to RF radiation.]

Karipidis *et al.* (2007) reported on risk of glioma in relation to occupational exposure to RF radiation in a case–control study in five major population centres in the Australian state of Victoria. Cases were patients aged 20–70 years with glioma, newly diagnosed between July 1987 and December 1991, who were ascertained by screening the medical records of 14 major Melbourne (capital of Victoria) hospitals that together provided most of the neurosurgical services in the state. Completeness of ascertainment was checked against cancer-registry records of Victoria. Controls were randomly selected from the electoral rolls and frequency-matched to cases by age and sex; the electoral rolls covered about 85% of citizens at that time. Controls were excluded if they had a history of brain tumour, stroke or epilepsy. Participants completed a self-administered work-history questionnaire, which included queries about occupation, employer, industry, main tasks and duties, equipment used, start and finish dates, number of hours worked per day, number of days worked per week and whether or not they had been exposed to RF radiation, for all jobs undertaken since age 12 years that had lasted ≥ 3 months. Work histories were checked for completeness at a subsequent face-to-face interview. For 44% of cases and 2% of controls, a next-of-kin proxy completed the work history. In addition to the self-report, exposure to RF radiation was assessed from the work history by use of the Finnish National Job-Exposure Matrix (FINJEM; a community-based job-exposure matrix developed by the Finnish Institute of Occupational Health) and by review of the work histories by an expert occupational hygienist. Four categories of cumulative exposure were created for each exposure measure: unexposed, and thirds of the ranked exposure distributions for all exposed subjects. Results were adjusted for age, sex and years of schooling (a surrogate for socioeconomic status). Data on occupational exposure were obtained for 414 cases and 421 controls, i.e. 66% and 65%, respectively, of those eligible and contactable [respective numbers not contacted were not given]. With FINJEM, 18 cases and 17 controls were classified as exposed to RF radiation, 29 and 48 by self-report and 33 and 25 by expert assessment. Only in the case of classification based on expert assessment of exposure was there any consistent indication that risk of glioma increased with exposure to RF radiation: relative to those who were not exposed, odds ratios were 1.20 (95% CI, 0.48–3.04) for > 0–3 years of exposure, 1.65 (95% CI, 0.66–4.17) for > 3–6 years and 1.57 (95% CI, 0.62–4.02) for > 6 years (Table 2.1). Analyses excluding participants with proxy information showed no major differences in results. [The use of multiple measures of occupational exposure to RF radiation, including expert assessment of a comprehensive occupational history, was a strength of the study. It was limited by lack of inclusion of non-contactable subjects when estimating participation rates, by the large proportion of

cases requiring proxy respondents and by the comparatively small number of subjects who were exposed to RF radiation. FINJEM provides a probably incomplete assessment of occupational exposure to RF radiation.]

Baldi *et al.* (2011) reported on a case–control study of people aged ≥ 16 years, newly diagnosed with cancer of the primary CNS between mid-1999 and mid-2001 in the administrative region of Gironde in south-western France. Patients with neurofibromatosis, Von Hippel-Lindau disease or AIDS were excluded. Controls were selected from local electoral rolls, which automatically register all French subjects, and individually matched to cases by age, sex and department of residence. Participation rates were 70% of eligible cases and 69% of eligible and contactable controls. Occupational exposure to RF radiation was assessed by two occupational hygienists from lifetime histories of jobs that had lasted ≥ 6 months (including job title, industry, dates each job began and ended, details of tasks performed), which were collected by face-to-face interview. Information on use of amateur radio was also collected. The odds ratio for occupational exposure to RF radiation and all tumours of the brain was 1.50 (95% CI, 0.48–4.70), while for use of amateur radio it was 1.39 (95% CI, 0.67–2.86) (Table 2.1). [The Working Group noted the comparatively small size of the study and the small number of exposed subjects, which appeared to have precluded analysis at multiple exposure levels; the exposure assessment based on a comparatively limited occupational history, and an estimated participation rate for controls that was not based on all potentially eligible participants.]

(b) Cohort studies

Lilienfeld *et al.* (1978) reported on a retrospective cohort study of USA employees and their dependents who had worked or lived at the United States embassy in Moscow during 1953–1976 and, for comparison, employees and their dependents at other United States embassies in eastern Europe who had not served in Moscow over the same period. There were unusual levels of background exposure to MW in the embassy in Moscow. The maximum measured levels were 5 μW/cm^2 for 9 hours per day, 15 μW/cm^2 for 18 hours per day, and < 1 μW/cm^2 thereafter for non-overlapping time periods between 1953 and 1975 and between 1975 and 1976. Only background levels of exposure to MW were recorded in other eastern-European embassies. Relevant health information and follow-up data were obtained from the medical records of employees and their dependents (held by the Department of State) and a health-history questionnaire sent to each employee or dependent who could be located. Death certificates were sought for all decedents. The analysis was based only on subjects who could be traced (> 90%): 1719 Moscow employees and 1224 dependents known to have lived with them in the embassy, and 2460 employees at other embassies and 2072 dependents known to have lived with them. For embassy employees, 194 deaths were ascertained; of these, there was sufficient information for 181 for inclusion in the analysis, and death certificates were available for 125. There were no deaths from tumours of the brain or other parts of the CNS in Moscow employees, compared with 0.9 expected on the basis of comparable mortality rates in the USA [standardized mortality ratio, SMR, 0; 95% CI, 0–4.1). For other embassy employees, there were five deaths from tumours of the brain or other parts of the CNS, with 1.5 expected (SMR, 3.3; 95% CI, 1.1–7.7). For dependents known to have lived in the relevant embassy, > 90% were traced, 67 deaths were ascertained, 62 death certificates were available. There were no observed deaths from tumours of the brain or other parts of the CNS (0.15 expected) [SMR, 0; 95% CI, 0–24.6] for the Moscow embassy and 1 death was observed (0.19 expected) for the other embassies (Table 2.2). [This study was available only in a United States government report; it was not published in the

peer-reviewed literature. Its main weaknesses were the small sizes of the two cohorts and the small number of deaths from cancer of the CNS observed. The long and continuous exposure to high background levels of MW in the Moscow Embassy was a strength. Possible confounding factors were not addressed.]

Milham (1988a, b) followed a cohort of people who were licensed as amateur radio-operators between 1 January 1979 and 16 June 1984 (a licence was valid for 5 years) and had addresses in Washington State or California. The full names and dates of birth of male cohort members (67 829 people; there were few females) were matched with deaths in Washington State and California. Only exact matches were accepted. Person-years at risk started on the effective current registration day and ended on the day of death, or on 31 December 1984. There were 232 499 person-years at risk and 2485 deaths; 29 deaths from cancer of the brain (International Classification of Disease Revision 8 [ICD-8] code 191) were observed and 20.8 expected [the death rates used to estimate the expected numbers were not specified], SMR for deaths from cancer of the brain was 1.39 (95% CI, 0.93–2.00) (Table 2.2). Licensees were further subdivided by licence class, i.e. Novice, Technician, General, Advanced and Extra. Novices were limited in their use of transmitter power and transmission frequencies; these conditions became more liberal as licence class rose. The average age increased with rising licence class; those holding higher-level licences may have generally been amateur radio operators for longer than those holding lower-level licences. Deaths from cancer of the brain were more frequent than expected for each licence class after Novice, but with little evidence of progressive increases as licence class rose (Table 2.2). [The main strength of this study was its clear and straightforward execution. Its weaknesses included lack of information about erroneous or missed links of cohort members to deaths, lack of consideration of possible migration of cohort members from Washington State and California, limited validation of licence class as a surrogate for intensity and duration of exposure to RF radiation, and the small number of observed deaths from cancer of the brain. Possible confounding factors were not addressed.]

Armstrong *et al.* (1994) carried out a nested case–control analysis of the association of several cancers, including tumours of the brain, and exposure to pulsed electromagnetic fields (PEMFs; frequency range, 5–20 MHz) in two cohorts of electrical-utility workers in Quebec, Canada (21 749 men; follow-up, 1970–1988), and France (170 000 men; follow-up, 1978–1989), among whom 2679 cases of cancer were identified, 84 malignant tumours of the brain and 25 benign tumours of the brain. Utility-based job-exposure matrices were created with information obtained from surveys of samples of 466 (Quebec) and 829 (France) workers wearing exposure meters in 1991–1992. For malignant tumours, the odds ratios were 0.84 (95% CI, 0.47–1.50) for above-median exposure to PEMFs and 1.90 (95% CI, 0.48–7.58) for exposure at or above the 90th percentile, while for astrocytoma – the most common type of glioma – the odds ratio for exposure at or above the 90th percentile was 6.26 (95% CI, 0.30–132). For benign tumours, the odds ratio was 1.58 (95% CI, 0.52–4.78) for above-median exposure. None of the odds ratios for other subtypes of cancer of the brain were elevated (Table 2.2).

Grayson (1996) reported on risk of brain cancer related to exposure to equipment producing RF or MW (RF/MW) radiation in a case–control study conducted within a cohort of male members of the United States Air Force in 1970–89 (Table 2.2). Four matched controls were randomly selected for each case from all cohort members. Controls were not eligible if they had been diagnosed with leukaemia, cancer of the breast or melanoma "...because excess risks of these tumours have been associated with EMF exposures in other studies" [this exclusion was

not appropriate in a nested case–control study as if the excluded tumours were associated with EMF exposure, this could bias exposure in controls downwards, though probably only to a very small degree given the relative rarity of these cancers]. An expert panel assessed each job title–time couplet for probability of exposure to RF/MW radiation, which was recorded as "unexposed," "possibly exposed" and "probably exposed." Incident cases of cancer of the brain (ICD-9 code 191) were identified from hospital discharge records of serving personnel; confirmatory data (imaging or histopathology records) were not sought. Conditional logistic regression was used for the analysis; no potential confounders were included as covariates in the models. The odds ratio for cancer of the brain with ever-exposure to RF/MW was 1.39 (95% CI, 1.01–1.90). There was only weak evidence of a trend towards increasing odds ratio with increase in the value of the product of a score for probable intensity of exposure and duration of exposure. [The strengths of this study included its basis within a cohort, the careful design and the probably complete ascertainment of brain cancers occurring within the study period. It is limited by its lack of confirmation of diagnosis through access to diagnostic records, the reliance on occupational title to identify instances of potential exposure to RF/EMF radiation, and the uncertain accuracy of exposure quantification. Any bias due to these weaknesses would probably be towards the null and would weaken a dose–response relationship, if there were one.]

Szmigielski (1996) studied the incidence of cancer in the whole population of career military personnel in Poland from 1971 to 1985, averaging about 127 800 men over these 15 years. [This study appeared to be a cross-sectional study rather than a cohort study (Table 2.2).] Annual data were obtained on all career servicemen from personnel and health departments, and included numbers of servicemen, types of service posts and exposure to possible carcinogenic factors during service, while military safety groups provided information on the number of personnel exposed to RF radiation. On average, 3720 men were considered to have been exposed to RF radiation each year. It was estimated that of these, 80–85% were exposed at < 2 W/m^2 and the remainder at 2–6 W/m^2, but individual exposure levels could not be assigned. Exposure was largely to pulse-modulated RF radiation at 150–3500 MHz. Annual data on all men newly diagnosed with cancer were collected from records of military hospitals and the military medical board; in addition to type of cancer, they included duration and type of service and exposure to possible carcinogenic factors during service, including whether or not they were exposed to RF radiation. [It was unclear from the text whether information in individual health records may have been used, in addition to information applicable to all servicemen, in allocating a man diagnosed with cancer to the group exposed to RF radiation.]

[It appeared to the Working Group that these data were insufficient to permit calculation of annual age-specific rates of all cancers (in age groups of 10 years) and individual types of cancer in men exposed to RF radiation and men not exposed and thus to calculate ratios of incidence in the exposed group to that in the unexposed group for each year and for the whole period. The methods were described in limited detail and it was not stated how the rates or rate ratios were summarized across age groups and years and, in particular, whether cancer-incidence rate ratios based on all exposed and all unexposed men were age-standardized. The observed numbers of cases of all cancers or individual types of cancer were not presented, but could be approximated from average annual rates of incidence, from which it appeared that two to three cases of cancer of the nervous system and brain (ICD codes not specified) were diagnosed in men exposed to RF radiation over the 15 years, and about 54 cases in men not exposed.]

Table 2.2 Cohort studies of cancer of the brain and occupational exposure to radiofrequency radiation

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Lilienfeld *et al.* (1978) United States embassies in eastern Europe	7475	1953–76	Worked or lived in the United States embassy in Moscow during study period. The maximum measured levels were 5 μW/cm^2 for 9 h/d, 15 μW/cm^2 for 18 h/d, and < 1 μW/cm^2 thereafter for non-overlapping periods between 1953 and 1975 and between 1975 and 1976	Brain and CNS (ICD-7 code 193)	*Role and location in eastern Europe*		SMR	Sex, age	SMRs are relative to the corresponding mortality rates in the USA. Contract report is available through the National Technical Information Service of the USA.
					Employed in the United States embassy in Moscow	0	0 [0–4.1]*		
					Dependent of a Moscow United States embassy employee	0	0 [0–24.6]*		
					Employed in a different United States embassy in eastern Europe	5	3.3 [1.1–7.7]*		
					Dependent of an employee at a different United States embassy in eastern Europe	1	5.3 [0.13–29]*		
Milham (1988a, b) USA	67 829	1979–84	Licensing as an amateur radio operator	Brain (191)	*Amateur radio operator licence class*		SMR		
					Novice	1	0.34		
					Technician	4	1.12		
					General	11	1.75		
					Advanced	11	1.74		
					Extra	2	1.14		
					All	29	1.39 (0.93–2.00)		

Table 2.2 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Armstrong *et al.* (1994) Canada and France	191 749	1970–89	Exposure assessed through a job-exposure matrix based on about 1000 person-weeks of measurements from exposure meters worn by workers to derive estimates of short-duration PEMFs, or high-frequency transient fields.	Brain (191)	*PEMFs*		OR	SES	Nested case–control analysis. Controls for each case were selected at random from the cases risk set and matched by utility and year of birth. Exposure was counted only up to the date of diagnosis of the case.
					Malignant cancer of the brain:				
					< Median	49	1.00		
					> Median	35	0.84 (0.47–1.50)		
					≥ 90th percentile	9	1.90 (0.48–7.58)		
					Astrocytoma:				
					< Median	22	1.00		
					> Median	12	0.89 (0.29–2.67)		
					≥ 90th percentile	3	6.26 (0.30–132)		
					Glioblastoma:				
					< Median	16	1.00		
					> Median	13	0.49 (0.19–1.28)		
					≥ 90th percentile	5	0.57 (0.08–3.91)		
					Other cancers:				
					< Median	7	1.00		
					> Median	6	2.67 (0.43–16.71)		
					≥ 90th percentile	1	-		
					Benign tumours of the brain:				
					< Median	9	1.00		
					> Median	16	1.58 (0.52–4.78)		
					≥ 90th percentile	1	-		

Table 2.2 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Grayson (1996) USA	230 cases, 920 controls	1970–89	Job title-time-exposure matrix. Census of control histories was carried out at time of matched case's diagnosis. Exposure score was the sum of the products of duration of deployment in each job and the assessed probability of RF exposure in that job at that time.	Brain (191)	*RF/MW*		OR	Controls exactly matched to case on year of birth, race and presence in the cohort at the time when the case was diagnosed. Matching retained in analysis. Age, race, rank (senior or other) included as covariates.	United States Air Force personnel Nested case–control analysis within cohort study. All male members of United States Air Force. Rank associated with risk; senior officers at increased risk.
					Never exposed	94	1.00		
					Exposed	136	1.39 (1.01–1.90)		
					RF/MW exposure score				
					None	136	1.00		
					2–48	15	1.26 (0.71–2.24)		
					49–127	29	1.50 (0.90–2.52)		
					128–235	25	1.26 (0.71–2.22)		
					236–610	25	1.51 (0.90–2.51)		
Szmigielski (1996) Poland	Average of 127 800 men, yearly during 15 yr	1971–85	Military safety (health and hygiene) groups classified military service posts as having exposure, or not, to RF	Nervous system, including brain	*Occupational exposure to RF*			None specified	Cross-sectional study. Incidence rate ratio for all cancers, 2.07 (95% CI, 1.12–3.58) suggests possible upward bias in rate ratios.
					Not exposed	[54]*	1.00		
					Exposed	[2–3]*	1.91 (1.08–3.47)		
					P value		< 0.05		
Tynes *et al.* (1996) Norway	2619 women	1961–91	Radio and telegraph operators with potential exposure to RF and ELF	Brain (ICD-7 code 193)	Radio and telegraph operators with potential exposure to RF and ELF	5	SIR, 1.0 (0.3–2.3)	Age, time since certification, calendar year, age at first childbirth	Women certified as radio and telegraph operators 1920–80

Table 2.2 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Lagorio *et al.* (1997) Italy	481 women	1962–92	Occupational history from plant records. RF generated by dielectric heat sealers. Exposure of 10 W/m^2 equivalent power-density frequently exceeded.	Brain (191)	*Job title*			Sex, age, calendar period-specific regional person-year at risk	Mortality analysis restricted to women
					RF-sealer operators	1	10 [0.25–56]*		
					Other workers	0	0 [0–46]*		
					All female workers	1	5 [0.13–28]*		
Morgan *et al.* (2000) USA	195 775 Motorola employees	1976–96	Job-exposure matrix	Brain/CNS	*Cumulative exposure to RF*		*Rate ratio*	Age, sex, and race for external comparisons; and age, sex, and period of hire for internal comparisons	All employees of Motorola; exposure from cellular phones not assessed. Definition of exposure categories unclear.
					None	34	1.00		
					< Median	7	0.97 (0.37–2.16)		
					≥ Median	10	0.91 (0.41–1.86)		
					Usual exposure to RF				
					None	38	1.00		
					Low	7	0.92 (0.43–1.77)		
					Moderate	3	1.18 (0.36–2.92)		
					High	3	1.07 (0.32–2.66)		
					Peak exposure to RF				
					None	34	1.00		
					Low	10	0.98 (0.50–1.80)		
					Moderate	3	0.70 (0.21–1.77)		
					High	4	1.04 (0.36–2.40)		
					Duration of exposure				
					None	44	1.00		
					≤ 5 yr	3	0.74 (0.22–1.84)		
					> 5 yr	4	0.99 (0.35–2.26)		
					Cumulative exposure to RF				
					Males-low	23	1.00		
					Males-high	8	1.11 (0.38–2.78)		
					Females-low	18	1.00		
					Females-high	2	0.58 (0.03–3.30)		

Table 2.2 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Groves *et al.* (2002) USA	40 581 men (271 women excluded)	1950–97	United States Navy personnel with potential for RF exposure; job classified as entailing low or high exposure	Brain (ICD-9 codes 191.0–191.9)	*Job-associated exposure to RF*		*SMR*	Age at cohort entry, attained age	White United States Navy (male) veterans of Korean War (1950–54)
					Low	51	1.01 (0.77–1.33)		
					High	37	0.71 (0.51–0.98)		
					Total cohort	88	0.86 (0.70–1.06)		
					Within-cohort comparison:				
					Low exposure	51	1.00		
					High exposure	37	0.65 (0.43–1.01)		
Degrave *et al.* (2009) Belgium	Military personnel (4417 men) in batallions equipped with radar, and 2932 controls	1968–2003	Exposure levels on the site where the battalion lived and worked were characterized, individual exposure assessment could not be conducted.	Cancer of eye, brain and nervous system (190–192)	Control cohort	2	1.00		Cause of death found for 71% of the men in the radar group and 70% in the control group.
					Radar-exposed	8	2.71 (0.42–17.49)		

* values calculated/deduced by the Working Group

d, day or days; ELF, extremely low-frequency electric and magnetic field; h, hour or hours; mo, month; MW, microwaves; OR, odds ratio; PEMFs, pulsed electromagnetic fields; RF, radiofrequency radiation; SES, socioeconomic status; SIR, standardized incidence ratio; SMR, standardized mortality ratio; W, watt; yr, year

The incidence rate ratio (IRR) for cancer of the nervous system and brain over the 15 years in those exposed to RF radiation was estimated to be 1.91 (95% CI, 1.08–3.47). The corresponding incidence rate ratio for all cancers was 2.07 (95% CI, 1.12–3.58). [The similarity of these two incidence rate ratios suggested the possibility of consistent upward bias in their estimation. It also appeared that the 95% confidence intervals had not been correctly calculated given their similar width and the large difference in the observed numbers on which they were based: 2–3 cancers of the nervous system and brain and about 32 cancers of all types.] Age-specific incidence rate ratios for all cancers ranged from 2.33 at age 20–29 years to 1.47 at age 50–59 years. [This was somewhat against the hypothesis that failure to standardize by age had increased the incidence rate ratios with exposure to RF radiation. The interpretation of this study was hampered by its cross-sectional design, in which risk of cancer was related only to current exposure to RF radiation; uncertainty about the accuracy of the classification of exposure; lack of a quantitative measure of exposure; lack of information on completeness of ascertainment of cancer incidence; lack of clarity concerning the analytical methods, including whether incidence rate ratios were age-standardized; and probable errors in the statistical analysis. Possible confounding factors were not addressed. The possibility that medical records accessed for men with cancer may have provided information that led them to being classified as exposed to RF radiation may explain the apparently high risks of cancer in men exposed to RF radiation in this study.]

Tynes *et al.* (1996) examined incidence of cancer in a cohort of 2619 Norwegian women who were certified as radio and telegraph operators between 1920 and 1980 (Table 2.2); 98% had worked on merchant navy ships. They were followed from 1961 to 1991 via the Norwegian cancer registry; 41 were lost to follow-up. Electric and magnetic fields were measured in the radio rooms of three older Norwegian ships. They were below detection levels at radio-frequencies at the operators' desks and were considered to be comparable to those found at normal Norwegian workplaces. The age- and calendar period-adjusted standardized incidence ratio (SIR) for cancers of the brain and nervous system (ICD-7 code 193) was 1.0 (95% CI, 0.3–2.3; based on five cases) with reference to the national Norwegian female population. [The strengths of this study were its homogeneous cohort and near-complete follow-up; its principal weaknesses were the small number of cases of brain cancer and the probably low exposure of the cohort to RF radiation. Possible confounding factors were not addressed.]

Lagorio *et al.* (1997) reported on mortality from all causes and from specific cancers in a group of 201 men and 481 women employed in a plastic-ware manufacturing facility in Grossetto, Italy, from 1962 to 1992 and followed until death, or until the end of 1992 (Table 2.2) Those lost to follow-up were considered to be alive at the end of 1992. Vital status and cause of death were ascertained from the registry office of the municipality of residence and death. Workers were classified into three groups: RF-sealer operators, other labourers and white-collar workers. RF-sealer operators received the greatest exposure to RF radiation. They were also exposed to vinyl chloride monomer due to its volatilization from polyvinyl chloride (PVC) sheets during sealing. At the end of follow-up, 661 subjects were alive, 16 had died and 5 were lost to follow-up [details of tracing methods were not given]. The mortality analysis was restricted to women, who were mostly employed in the manufacturing department (6772 person-years in RF-sealer operators). There was one death ascribed to a tumour of the brain and 0.2 expected based on mortality rates in the regional population; this single death occurred in an RF-sealer operator (expected, 0.1). [The principal weakness of this study was its

small size. Possible confounding from exposure to vinyl chloride was not addressed.]

Morgan *et al.* (2000) studied a cohort of all employees of Motorola USA with at least 6 months of cumulative employment, who were employed for at least 1 day between 1976 and 1996, and followed to 31 December 1996. Deaths were ascertained through reference to the Social Security Administration Master Mortality File and the National Death Index. Death certificates were obtained from the state vital statistics offices and company benefits records, and causes of death were coded according to ICD-9. There were 195 775 workers, 2.7 million person-years of follow-up and 6296 deaths, 53 of which were attributed to cancer of the CNS [ICD-9 codes not stated]. No losses to follow-up were reported [it is probable that the 116 700 workers who had retired or whose employment had been terminated were assumed to be alive if no death record was found for them]. Exposure to RF radiation was assessed on the basis of a company-wide job-exposure matrix, developed through expert consultation, that categorized each of 9724 job titles into one of four exposure groups: background, low, moderate, and high, corresponding roughly to < 0.6 W, 0.6– < 2.0 W, 2.0– < 5.0 W, 5.0– < 50 W and ≥ 50 W. About 45 500 employees were thought to have had usual exposures of ≥ 0.6 W, 8900 employees had a high usual exposure (≥ 50 W) and 9000 employees had unknown usual exposure. Relative to mortality in the combined populations of Arizona, Florida, Illinois, and Texas, where most Motorola facilities were located, the SMR for tumours of the CNS was 0.60 (95% CI, 0.45–0.78). Internal comparisons between categories of estimated cumulative, usual and peak exposure to RF radiation; duration of exposure; (cumulative exposure lagged 5, 10 and 20 years) and cumulative exposure in males and females separately, showed no consistent evidence of an increase in risk of tumours of the CNS with increasing estimated exposure to RF radiation (Table 2.2). [The main strength of this study was the clear and straightforward execution and comprehensive analyses. Its weaknesses included lack of measured exposure to RF radiation on which to base the exposure classification; inadequate description of the exposure-validation study; lack of detail on how the links between cohort members and death records were established, and therefore uncertainty about completeness and accuracy of death ascertainment; the comparatively small number of observed deaths from tumours of the CNS; and possible conservative bias due to exclusion of mobile-phone use from the estimate of exposure to RF radiation. Possible confounding factors were not addressed.]

Groves *et al.* (2002) reported on an extended follow-up to death or to the end of 1997 for 40 890 United States Navy personnel originally studied by Robinette *et al.* (1980). These men were graduates of Class-A Navy technical training schools who had served on ships in the Korean War during 1950–54, and who had potentially been exposed to high-intensity radar. They were divided into two occupational groups considered by a consensus of Navy personnel involved in training and operations to have had high exposure to RF radiation (electronics, fire-control and aviation-electronics technicians: 20 109 men) or low exposure (radiomen, radar men and aviation electricians' mates: 20 781 men). Potential exposure in each job category was evaluated from the records for 435 men who had died and those of a randomly selected 5% of living men as "the sum of all power ratings of all fire control radars aboard the ship or search radars aboard the aircraft to which the technician was assigned multiplied by the number of months of assignment." Ascertainment of death required use of Department of Veterans' Affairs and Social Security Administration records and the National Death Index. [Its completeness was uncertain.] It was necessary to impute moderate proportions of dates of entry into the cohort (1950–54) and dates of birth, because of missing

data. The analysis was limited to 40 581 men and SMRs were calculated with reference to all white men in the USA, standardized for age at entry to the cohort and attained age. Altogether, there were 51 deaths from cancer of the brain (ICD-9 codes 191.0–191.9); there was no evidence of any increase in risk of cancer of the brain associated with high exposure to RF radiation (Table 2.2). The SMRs for cancer of the brain were 0.86 (95% CI, 0.70–1.06) for the whole cohort, 1.01 (95% CI, 0.77–1.33) for the group with low exposure to RF radiation (usual exposures well below 1 mW/cm^2) and 0.71 (95% CI, 0.51–0.98) for the group with high exposure to RF radiation (potential for exposures up to 100 kW/cm^2, but usually less than 1 mW/cm^2). Within the cohort, the relative risk (RR) of death from cancer of the brain in the group with high exposure to RF radiation relative to the group with low exposure was 0.65 (95% CI, 0.43–1.01). [This appeared to have been an initially somewhat poorly documented cohort, for which follow-up was difficult and some missing data, including birth date, had to be imputed. While expert assessment permitted division of the cohort into groups with low and high exposure to RF radiation, no specific measurements of exposure were reported. Assessment of exposure appeared to have been limited to 1950–54. Possible confounding factors, such as occupational exposure to other agents, were not addressed.]

In a cohort of 4417 Belgian male professional military personnel who served in battalions equipped with radar for anti-aircraft defence, cause-specific mortality was compared with that of 2932 Belgian military personnel who served in battalions not equipped with radar (Degrave *et al.*, 2009). Administrative archives of the battalions were used to reconstruct a list of personnel serving in each battalion. Lists were matched to those of the Department of Human Resources of the Belgian Army to find the subjects' birthdays, which allowed retrieval of their Belgian national identity number. With this number, mortality follow-up could be conducted. For military personnel who died before 1979, the registry only recorded month and year of birth, and thus for 35 dead military exact birth-dates were not available, matching was equivocal and the cause of death was not used. The registry was complete until 1997 and from 1998 to 2004, only for the northern, Dutch-speaking part of Belgium. In parallel, for all professional military personnel who died up to 31 December 2004, first-degree family members were sought and a questionnaire sent to enquire about likely cause of death. For the period of follow-up of this study, the Belgian cancer registry was incomplete, but the information on cases of cancer reported to the registry was reliable. Thus the cancer registry was used only for confirmation, but not for identification of cancer cases. The risk ratio for deaths from cancers of the eye, brain and nervous system in the cohort serving in battalions equipped with radar compared with the unexposed cohort was 2.71 (95% CI, 0.42–17.49) (Table 2.2). [The Working Group noted the difficulties in following-up the study population that may have affected the study results, as well the difficulty of attributing any possible increase in risk ratio to exposure to RF radiation, given possible confounding due to ionizing radiation also emitted by devices producing MW radiation.]

2.1.2 Leukaemia and lymphoma

(a) Case–control studies

No data were available to the Working Group.

(b) Cohort studies

Lilienfeld *et al.* (1978) reported on a retrospective cohort study of USA employees, and their dependents, who had worked or lived at the United States embassy in Moscow during 1953–76 (see Section 2.1.1 for details). The total risk ratio for leukaemia in the embassy employees was 2.5 (95% CI, 0.3–9.0).

Milham (1988a, b) followed a cohort of people who were licensed as amateur radio operators between 1 January 1979 and 16 June 1984 (see Section 2.1.1 for details). There was a borderline excess risk of death from lymphatic and haematopoietic neoplasms, from acute myeloid leukaemia, and from multiple myeloma and lymphoma (Table 2.3). There was no evidence for an increase in SMR for these neoplasms with higher license class (see Section 2.1.1. for discussion of the strengths and weaknesses of this study).

Armstrong *et al.* (1994) conducted a nested case–control study of cancers at different sites within cohorts of electrical workers in Quebec, Canada, and in France (see Section 2.1.1 for details). There were no excess risks for all haematological cancers, non-Hodgkin lymphoma (NHL) or for all leukaemias, or for any of the subtypes of leukaemia, associated with exposure to PEMF (Table 2.3). [The strengths and weaknesses of this study are described in Section 2.1.1.]

The study by Szmigielski (1996) is described in detail in Section 2.1.1. A significantly increased incidence rate ratio for cancers of the haematological system and lymphatic organs was reported (Table 2.3). [The results were difficult to interpret, as there were many methodological flaws in the design and analysis of the study. Main issues were that exact data on the age of the subjects in the cohort were missing and that collection of exposure data was potentially differential.]

Tynes *et al.* (1996) followed a cohort of 2619 Norwegian women who were certified as radio and telegraph operators between 1920 and 1980. There was no elevation in risk of lymphoma or leukaemia for those potentially exposed to RF radiation (Table 2.3). [The strengths of this study are discussed in Section 2.1.1; its principal weaknesses were the small number of cancer cases and the probably low exposure of the cohort to RF radiation. Possible confounding factors were not addressed.]

Lagorio *et al.* (1997) reported on mortality from all causes and from specific cancers in a group of plastic sealers in Italy (see Section 2.1.1 for details). There was one death (0.2 expected) ascribed to leukaemia in an RF-sealer operator (Table 2.3). [The principal weakness of this study was its small size. Possible confounding factors were not addressed.]

Morgan *et al.* (2000) reported on a 20-year follow-up of 195 775 employees of Motorola USA (described in Section 2.1.1) and considered death from lymphatic and haematopoietic malignancies (Table 2.3). Of these, there were 87 deaths from leukaemia, 19 from Hodgkin disease and 91 from NHL. Reduced odds ratios for lymphatic and haematopoietic malignancies and subtypes were seen among workers categorized as exposed (compared with non-exposed workers) in most categories of estimated exposure, duration of exposure and cumulative exposure lagged 5, 10 and 20 years. [The Working Group noted the small number of deaths from lymphoma and leukaemia in the exposed cohort, which, together with the other limitations mentioned in Section 2.1.1, complicated the interpretation of these findings.]

Richter *et al.* (2000) collected data on six patients claiming compensation for their cancer who visited the Unit of Occupational and Environmental Medicine at the Hebrew University-Hatlawah Medical School, Jerusalem in 1992–99. They were judged to have received high RF/MW radiation based on self-reports, information from manuals containing specifications of the equipment they had used and repaired, and results of sporadic measurements from their work and medical records. A study was then conducted of 25 co-workers of one of the patients and of other personnel with self-reported exposure to RF radiation. An increased risk of haematolymphatic malignancies was found (5 cases observed compared with 0.02 cases expected among Jewish men aged 20–54 years). [The Working Group noted that the results of

this study were very difficult to interpret, due to unclear definition of the study population, follow-up and exposure assessment.]

Groves *et al.* (2002) reported on mortality in a cohort of 40 890 male United States Navy personnel who had served on ships during the Korean War in 1950–54 in an extended follow-up to 1997 (described in more detail in Section 2.1.1). The cohort was divided into two subgroups on the basis of job title, with potential exposure to RF radiation based on expert assessment: 20 109 workers comprising a subcohort with high exposure to RF radiation (potential for exposures up to 100 kW/cm^2, but usually < 1 mW/cm^2) and a subcohort of 20 781 workers with low exposure (usually well below 1 mW/cm^2). A total of 182 deaths from lymphoma or multiple myeloma (91 each in the high- and low-exposure subcohorts) and 113 deaths from leukaemia (44 and 69 in the high- and low-exposure subcohorts, respectively) were identified in 1950–97. In both subcohorts, SMRs were not elevated for lymphoma and multiple myeloma, all leukaemias, lymphocytic leukaemia or non-lymphocytic leukaemia (Table 2.3). An internal comparison of high relative to low exposure to RF radiation elicited RRs of 0.91 (95% CI, 0.68–1.22) for lymphoma and multiple myeloma, 1.48 (95% CI, 1.01–2.17) for all leukaemias, 1.82 (95% CI, 1.05–3.14) for non-lymphocytic leukaemia and 1.87 (95% CI, 0.98–3.58) for acute non-lymphocytic leukaemia. An increased risk of all leukaemias was observed primarily in aviation-electronics technicians (RR, 2.60; 95% CI, 1.53–4.43, based on 23 deaths) and was highest for acute myeloid leukaemia (RR, 3.85; 95% CI, 1.50–9.84, based on 9 deaths). RRs for other job categories with high exposure were close to 1. This was interpreted as indicating a possible association, since aviation-electronics technicians who dealt primarily with mobile radar units may have had more potential to enter the beam path of an operating radar than members of other groups who worked with ship-mounted radars. [The limitations of this study are discussed in Section 2.1.1, including limitations in the documentation of the cohort definition and difficulties in follow-up. Classification of exposure to RF radiation in the different groups was based on expert assessment. No measurement of RF radiation was provided.]

Degrave *et al.* (2009) compared a cohort of 4417 Belgian male professional military personnel who served in battalions equipped with radars for anti-aircraft defence with 2932 Belgian male professional military personnel who served at the same time in the same place in battalions not equipped with radars. Attempts were made to characterize exposure levels on the site where the battalion lived and worked, but individual exposure assessment could not be conducted. Administrative archives of the battalions were used to reconstruct a list of personnel serving in each battalion. These archives only provided first name, family names, and a unique identification number. Lists were matched to those of the Department of Human Resources of the Belgian Army to find the subjects' birthdays, which allowed retrieval of their Belgian national identity number. With this number, mortality follow-up could be conducted. The first source of information on cause of death was the official Belgian death registry, which collects anonymous data. Linkage was conducted using date of birth and date of death as matching variables (cause of death could be found for 71% of persons in the radar group and 70% in the control group). For military personnel who died before 1979, the registry only recorded month and year of birth, and exact birth-dates were not available for 35 of the dead, while matching was equivocal and the cause of death was not used. The registry was complete until 1997 and from 1998 to 2004, only for the Northern, Dutch-speaking part of Belgium. In parallel, for all professional military personnel who died up to 31 December 2004, first-degree family members were sent a questionnaire to enquire about the likely cause of death. For the period of follow-up of this study,

Table 2.3 Cohort studies of leukaemia and occupational exposure to radiofrequency radiation

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Lilienfeld *et al.* (1978)	7475	1953–76	Worked or lived in the United States embassy in Moscow during study period. The maximum measured levels were 5 μW/cm^2 for 9 h/d, 15 μW/cm^2 for 18 h/d, and < 1 μW/cm^2 thereafter for non-overlapping periods 1953–1975 and 1975–1976	Leukaemia	Embassy employees		2.5 (0.3–9.0)	Sex, age	SMRs are relative to the corresponding mortality rates in the USA. Contract report is available through the National Technical Information Service of the USA.
Milham (1988a, b) USA	67 829	1979–1984	Licensing as an amateur radio operator	Lymphatic and haematopoietic cancers			*SMR*		The death rates used to estimate the expected numbers were not specified
					All leukaemia	89	1.23 (0.99–1.52)		
					AML	36	1.24 (0.87–1.72)		
					Multiple myeloma and lymphoma	15	1.76 (1.03–2.85)		
					All lymphatic and haematopoietic cancers	43	1.62 (1.17–2.18)		
					By licence class:				
					Novice	9	1.01 [0.46–1.92]*		
					Technician	18	1.63 [0.97–2.58]*		
					General	26	1.19 [0.78–1.74]*		
					Advanced	27	1.15 [0.76–1.67]*		
					Extra	9	1.34 [0.61–2.54]*		

Table 2.3 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Armstrong *et al.* (1994) Canada and France	191 749	1970–89	Exposures assessed through a job-exposure matrix based on about 1000 person-weeks of measurements from exposure meters worn by workers to derive estimates of short-duration PEMFs, or high-frequency transient fields.	Haematological	*PEMFs*		OR	SES	Nested case–control analysis Controls for each case were selected at random from the cases risk set, and matched to the case by utility and year of birth. Exposure was counted only up to the date of diagnosis of the case.
					All haematological cancers:				
					< Median	167	1.00		
					> Median	135	0.90 (0.65–1.25)		
					≥ 90th percentile	28	0.96 (0.48–1.90)		
					NHL:				
					< Median	54	1.00		
					> Median	56	1.41 (0.83–2.38)		
					≥ 90th percentile	13	1.80 (0.62–5.25)		
					All leukaemias:				
					< Median	57	1.00		
					> Median	38	0.69 (0.40–1.17)		
					≥ 90th percentile	9	0.80 (0.19–3.36)		
Szmigielski (1996) Poland	Average of 127 800 men, yearly during 15 yr	1971–85	Military safety (health and hygiene) groups classified military service posts as having exposure, or not, to RF	Cancer of the haematopoietic system and lymphatic organs	*Occupational exposure to RF*		Incidence rate ratios	None specified	Cross-sectional study
					Not exposed	[131]*	1.00		
					Exposed	[24]*	6.31 (3.12–14.32)		
Tynes *et al.* (1996) Norway	2619 women	1961–91	Radio and telegraph operators with potential exposure to RF and ELF fields	Lymphoma (ICD-7 code 201) Leukaemia (ICD-7 code 204)	*Potential exposure*		*SIR*	Age, time since certification, calendar year, age at first childbirth	Women certified as radio and telegraph operators, 1920–80
					Lymphoma	5	1.3 (0.4–2.9)		
					Leukaemia	2	1.1 (0.1–4.1)		

Table 2.3 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Lagorio *et al.* (1997) Italy	481 women	1962–92	Occupational history from plant records. RF generated by dielectric heat sealers. Exposure of 10 W/m^2 equivalent power-density frequently exceeded.	Leukaemia (204–208)	*Job title* RF-sealer operators Other workers All female workers	 1 1 2	*SMR* [5.0 (1.27–27.85)]* [11.1]* 8.0 (1.0–28.8)	Sex, age, calendar period-specific regional person-year at risk	Mortality analysis; restricted to women
Richter *et al.* (2000) Israel	Co-workers (n = 25) of one of the six patients claiming compensation for their cancer, and other personnel with self-reported exposure to RF	1992–99	Self-reports, information from manuals containing specifications of the equipment they had used and repaired, and results of sporadic measurements from their work and from medical records.	Haemato-lymphatic malignancies	Jewish men aged 20–54 yr	5	*SIR* [250 (81.17–583.42)]*	None	[The Working Group noted that the results of this study were very difficult to interpret, due to unclear definition of the study population, follow-up, and exposure assessment.]

Table 2.3 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Morgan *et al.* (2000) USA	195 775	1976–96	Job-exposure matrix, developed through expert consultation that categorized each of 9724 job titles into different RF exposure groups: background, low, moderate, and high, corresponding roughly to < 0.6 W, 0.6 to < 2.0 W, 2.0 to < 5.0 W, 5.0 to < 50 W and ≥ 50 W, respectively	All lymphatic/ haematopoietic cancers (n = 203)	*Cumulative exposure to RF*		Rate ratio	Age, sex, and race for external comparisons; and age, sex, and period of hire for internal comparisons	All employees of Motorola; exposure from cellular telephones not assessed. Definition of exposure categories unclear
					None	148	1.00		
					< Median	21	0.74 (0.39–1.28)		
					> Median	34	0.67 (0.40–1.05)		
					Usual exposure to RF				
					None	152	1.00		
					Low	28	0.94 (0.57–1.47)		
					Moderate	10	0.90 (0.39–1.78)		
					High	8	0.70 (0.27–1.47)		
					Peak exposure to RF				
					None	145	1.00		
					Low	34	0.79 (0.49–1.23)		
					Moderate	11	0.58 (0.25–1.13)		
					High	10	0.60 (0.49–1.23)		
					Duration of exposure				
					None	182	1.00		
					≤ 5 yr	5	0.29 (0.12–0.57)		
					> 5 yr	16	0.89 (0.55–1.35)		
					Cumulative exposure to RF				
					Males-low	109	1.00		
					Males-high	19	0.53 (0.39–0.72)		
					Females-low	60	1.00		
					Females-high	15	1.12 (0.22–3.90)		

Table 2.3 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Groves *et al.* (2002) USA	40 581 men (271 women excluded)	1950–97	United States Navy personnel with potential exposure to RF; job classified as having low or high exposure by a consensus of Navy personnel involved in training and operation	All haematopoietic cancers (200–208)	*Job-associated exposure to RF*		*SMR*	Age at cohort entry and attained age	White (male) United States Navy veterans of Korean War (1950–54) Reference: all white men, USA Group of aviation-electronics technicians: RR 2.60 (1.53–4.43) for all leukaemias; RR 3.85 (1.50–9.84) for acute myeloid leukaemia
					Lymphoma and multiple myeloma:				
					Low	91	0.94 (0.77–1.16)		
					High	91	0.89 (0.72–1.09)		
					All leukaemias:				
					Low	44	0.77 (0.58–1.04)		
					High	69	1.14 (0.90–1.44)		
					Lymphocytic leukaemia:				
					Low	17	1.31 (0.81–2.11)		
					High	16	1.12 (0.69–1.83)		
					Non-lymphocytic leukaemia:				
					Low	20	0.67 (0.43–1.04)		
					High	39	1.24 (0.90–1.69)		

Table 2.3 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Degrave *et al.* (2009) Belgium	Military personnel (4417 men) in batallions equipped with radar, and 2932 controls	1968–2003	Exposure levels on the site where the battalion lived and worked were characterized; individual exposure assessment could not be conducted.	Cancer of lymphatic and haematopoietic tissue (200–208)	Control cohort Radar exposed	1 11	1.00 7.22 (1.09–48.9)		Cause of death found for 71% of the men in the radar group and 70% in the control group

* values calculated/deduced by the Working Group

AML, acute myeloid leukaemia; ELF, extremely low frequency electric and magnetic field; MW, microwaves; NHL, non-Hodgkin lymphoma; OR, odds ratio; PEMFs, pulsed electromagnetic fields; RF, radiofrequency radiation; SES, socioeconomic status; SIR, standardized incidence ratio; SMR, standardized mortality ratio; W, watt; yr, year

the Belgian cancer registry was extremely incomplete, but the information on cases of cancer reported to the registry was reliable. Thus, the cancer registry was used only for confirmation but not for identification of cancer cases. The relative risks were estimated, adjusting for age in 10-year categories with a Poisson regression model. There were 11 deaths from lymphatic and haematopoietic neoplasms in the radar battalion compared with 1 in the unexposed cohort (RR, 7.22; 95% CI, 1.09–48.9) (Table 2.3). [The Working Group noted the difficulties in following-up the study population, which may have affected the study results, as well the difficulty in attributing any possible increase in relative risk to exposure to RF radiation, given possible confounding due to ionizing radiation also emitted by devices producing MW radiation.]

2.1.3 Uveal (ocular) melanoma

Stang *et al.* (2001) conducted population-based and hospital-based case–control studies of uveal melanoma and occupational exposures to different sources of electromagnetic radiation, including RF radiation. For the population-based study, 37 cases were identified by a reference pathologist (response rate, 84%) and 327 controls were sampled and matched from the same region of residence, age and sex (response rate, 48%). For the hospital-based study, the 81 cases were patients treated at the University of Essen (response rate, 88%) and controls (n = 148) were patients with benign intra-ocular tumours (response rate, 79%). The results of these studies were pooled.The 118 female and male cases and 475 controls were interviewed by a trained interviewer with a structured questionnaire involving medical history, lifestyle, occupation and occupational exposure to RF radiation. Participants were specifically asked about exposure to radar and to other RF-emitting devices ("Did you use radio sets, mobile phones or similar devices at your workplace for at least several hours per day?") and more detail was obtained from those who reported exposure. Additional information provided by exposed participants was used by two of the authors, working independently and unaware of case or control status, to classify them as: exposed only to radio receivers that do not transmit RF radiation and therefore unexposed; exposed to RF radiation from walkie-talkies and radio sets; possibly exposed to RF radiation from mobile phones; and probably or certainly exposed to RF radiation from mobile phones. Few participants reported occupational exposure to radar. The odds ratio for uveal melanoma was 0.4 (95% CI, 0.0–2.6). For exposure to radio sets, the odds ratio was 3.3 (95% CI, 1.2–9.2) (Table 2.4). Adjustment for socioeconomic status or iris/hair colour did not alter these results. The results for reported occupational use of mobile phones are considered in Section 2.3. [This study was weakened by its poor assessment of occupational exposure to RF radiation, particularly the retrospective classification of exposure to other RF-emitting devices, although neither should be a source of positive bias. Confounding of occupational exposure to RF radiation with exposure to ultraviolet light from the sun or other sources was not considered and may have been important if, for example, much of the use of radio sets had entailed use of walkie-talkie radios for communication outdoors.]

2.1.4 Cancer of the testis

(a) Case–control studies

Interpretable results were available from only two case–control studies (Table 2.5). Both were limited by reliance on self-report for exposure classification.

Hayes *et al.* (1990) carried out a case–control study in the USA examining associations of testicular cancer with occupation and occupational exposures. Cases (n = 271) were aged 18–42 years and diagnosed between 1976 and 1981 in three medical institutions, two of which

treated military personnel, while the controls (n = 259) were men diagnosed in the same centres with a cancer other than of the genital tract. A complete occupational history was taken and participants were also asked about specific exposures, including to radar equipment and to MW radiation, MW ovens or other radio-waves. For all cancers of the testis combined, the odds ratio associated with exposure to MW radiation, MW ovens or other radio-waves was significantly increased, while the odds ratio for exposure to radar equipment was not elevated (Table 2.5). The participants were further classified by an industrial hygienist as to degree of exposure to MW radiation, MW ovens, and other radio-waves and no indication of an exposure–response relationship was found. [The Working Group noted that the exposure-classification approach was based on self-report and was probably subject to substantial misclassification.]

Baumgardt-Elms *et al.* (2002) carried out a case–control study examining the association of cancer of the testis with workplace exposures to EMF. The histologically confirmed cases (n = 269; including 170 seminomas and 99 non-seminomas) were recruited between 1995 and 1997 from five German regions (response rate, 76%). The controls (n = 797) were randomly selected from mandatory registries of residents, with matching on age and region (response rate, 57%). Occupational exposure to EMF was assessed in standardized face-to-face interviews with closed questions. For radar, job descriptions were selected for participants who had reported exposure to radar or had worked in occupations and industries involving such exposures. The participants were classified as to exposure to radar on the basis of expert review and measurements conducted in Germany. There was no excess risk of cancer of the testis associated with being classified as having exposure to radar. [A comparison of self-report of exposure with classification by the expert panel showed substantial misclassification from reliance on self-report.]

(b) Cohort study

Davis & Mostofi (1993) reported six cases of cancer of the testis in a cohort of 340 police officers who used hand-held radar guns in the state of Washington, USA. Only one case was expected, based on national data. [The Working Group noted that the finding of the six cases as a cluster had sparked the investigation. Exposure assessments were not made for the full cohort.]

2.1.5 Other cancers

Armstrong *et al.* (1994) carried out a nested case–control study of the association between exposure to PEMFs and various cancers, including lung (described in Section 2.1.1). An association was observed between exposure to PEMFs and cancer of the lung (Table 2.6). The highest excess risk was found in cases first exposed 20 years before diagnosis. [The relevance of the measured EMF parameters to exposure to RF radiation was unclear.]

No association of RF radiation with cancer of the lung has been reported in other studies (Milham, 1988a; Szmigielski, 1996; Tynes *et al.*, 1996; Lagorio *et al.*, 1997; Morgan *et al.*, 2000; Groves *et al.*, 2002; Degrave *et al.*, 2009; described in Section 2.1.1, and Table 2.6). A later overview by Szmigielski *et al.* (2001) reported an incidence rate ratio of 1.06 in the population studied by Szmigielski (1996), based on 724 not-exposed cases and 27 exposed cases.

Tynes *et al.* (1996) (described in Section 2.1.1) studied the impact of exposure to RF radiation (405 kHz to 25 MHz) in an occupational cohort of Norwegian female radio/telegraph operators who had worked at sea for extended periods. There were increased standardized incidence ratios (SIR) for cancers of the breast and uterus (Table 2.6). A nested case–control analysis for cancer of the breast was performed within this cohort. To control for the possible confounding effect of reproductive history, the investigators linked the cohort to a unique database from

the Norwegian Central Bureau of Statistics that contained information on the reproductive histories of Norwegian women born between 1935 and 1969. After adjusting for duration of employment, the odds ratio for cancer of the breast was 4.3 (95% CI, 0.7–26.0) in women aged ≥ 50 years who had performed a large amount of shift-work (> 3.1–20.7 category–years). Adjustment for shift-work and relevant reproductive history reduced the odds ratio for cancer of the breast to 1.1 (95% CI, 0.2–6.1) in those with the longest duration of employment. [The apparent excess risk of cancer of the breast in this cohort, based on high-quality databases and linkage, was not explained by reproductive history and could be potentially attributed to exposure to light at night.]

2.2 Environmental exposure from fixed-site transmitters

Ecological studies are considered to provide a lower quality of evidence than case–control or cohort studies, as they reflect the possibility of uncontrolled confounding and possible misclassification of exposure. With regard to exposure to RF radiation and its association with cancers of the brain, there appears to be little possibility of confounding by anything other than socio-demographic factors associated with diagnostic opportunity. For other cancer sites, confounding may be of greater concern.

Individual measurements of distance from a transmitter as a proxy for exposure are effectively ecological measures, in which the ecological unit includes everyone living at the same distance, or within a restricted range of distances, from the transmitter. Spot measurements will only be partly correlated with total exposure and even a personal exposure meter provides only an approximation of the dose of radiation absorbed by a specific tissue. Measurement of lifetime exposure is problematic regardless of the study design, particularly when there is a high level of population mobility and measurements of exposure are not readily available for previous areas of residence.

The crucial issue is to what extent the exposure surrogate is associated with the radiation absorbed, since this modulates the statistical power of the study. Some studies have validated correlations between proxy measures, based either purely on distance or on a more sophisticated propagation model. In some cases the correlation has been estimated at approximately 60%, in others it is < 10%, especially when based upon self-report of exposures (Schmiedel *et al.*, 2009; Viel *et al.*, 2009; Frei *et al.*, 2010). Hence it is difficult to assume that exposure classification based on distance-based proxy measurements is useful, unless validation measurements are included. Detailed modelling of field propagation shows that several parameters are potentially required.

2.2.1 Cancer of the brain

(a) Ecological studies

In several ecological studies, incidence or mortality rates of brain tumours have been compared between defined populations living close to television or radio broadcast stations or other RF radiation fixed-site transmitters or transmission towers.

Selvin *et al.* (1992) undertook a cross-sectional analysis in which the proportion of people aged < 21 years with cancer of the brain diagnosed between 1973 and 1978 living ≤ 3.5 km or > 3.5 km from a large MW transmission tower (Sutro Tower) in San Francisco, USA (n = 35) was compared with corresponding proportions from the 1980 USA census. The odds ratio for cancer of the brain and living ≤ 3.5 km from the tower was 1.16 [95% CI, 0.56–2.39]. [No possible confounding factors were considered, nor were the ambient levels of RF radiation in the compared areas documented.]

Table 2.4 Case–control study of uveal melanoma and occupational exposure to radiofrequency radiation

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Stang *et al.* (2001) Germany, 1995–98	118 (37/81)	475	Population-based study: 327 controls sampled and matched from the same region of residence, age, and sex. Hospital-based study: controls were 148 patients with benign intraocular tumours.	Interviewer-administered structured questionnaire	Uveal melanoma	Radar units Radio set: Ever exposed Exposed ≥ 5 yr before Exposed for ≥ 3 yr	1 9 9 7	0.4 (0.0–2.6) 3.3 (1.2–9.2) 3.3 (1.2–9.2) 2.5 (0.8–7.7)	Age, sex, region, SES, colour of iris and hair	Results of the population-based study (37 cases) and the hospital-based study (81 cases) were pooled.

SES, socioeconomic status; yr, year

Table 2.5 Case–control studies of cancer of the testis and occupational exposure to radiofrequency radiation

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hayes *et al.* (1990) USA, 1976–81	271	259	Non-genital cancer, diagnosed in same hospital	Interviews, including a complete occupational history. Participants were queried on specific exposures including radar equipment and MW radiation, MW ovens or other radio-waves. In-person interviews were held in the hospital with 69% of the cases and with 71% of the controls, and over the telephone at home with the rest of the cases and controls.	Testicular seminoma (n = 60) Other germinal (n = 206) Non-germinal (n = 5)	*Radar equipment* Seminoma Other Total *Other MW/RF* Seminoma Other Total Based on job title: None Low Medium High	 12 30 NR 7 24 NR 116 10 6 12	 1.3 (0.6–2.8) 1.1 (0.6–1.9) 1.1 (0.7–1.9) 2.8 (0.9–8.6) 3.2 (1.4–7.4) 3.1 (1.4–6.9) 1.0 2.3 (0.6–9.4) 1.0 (0.3–3.8) 0.8 (0.3–2.0)	Age	Self-reported exposure Two of the three centres treated military personnel Poor agreement between self-reporting and job title No response rates reported

Table 2.5 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Baumgardt-Elms *et al.* (2002) Germany, 1995–97	269	797	Controls were randomly selected from mandatory registries of residents, and matched on age and region (response, 57%).	Interviewer-administered standardized questionnaire	Testicular (170 seminoma and 99 non-seminoma)	*Radar units*	22	1.0 (0.60–1.75)		Exposure to RF weighted by duration and distance from source
						RF emitters	50	0.9 (0.60–1.24)		
						Radar units				
						0	251	1.0		
						> 0 to ≤ 45	7	1.4 (0.55–3.77)		
						> 45 to ≤ 135	4	0.5 (0.17–1.55)		
						> 135 to ≤ 2225	7	0.9 (0.36–2.19)		
						RF emitters				
						0	220	1.0		
						> 0 to ≤ 6	19	1.0 (0.56–1.74)		
						> 6 to ≤ 15	14	0.7 (0.38–1.35)		
						> 15 to ≤ 102	16	0.9 (0.46–1.56)		

MW, microwave; NR, not reported; RF, radiofrequency radiation

Table 2.6 Cohort studies of cancers of the lung and other sites and occupational exposure to radiofrequency radiation

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Milham (1988a, b) USA	67 829	1979–84	Licensing as an amateur radio operator	Cancer of the respiratory system (160–163)	None	209	SMR, 0.66 (0.58–0.76)		The death rates used to estimate the expected numbers were not specified
Armstrong *et al.* (1994) Canada and France	191 749	1970–89	Exposures assessed through a job-exposure matrix based on about 1000 person-wks of measurements from exposure meters worn by workers to derive estimates of short-duration PEMFs, or high-frequency transient fields.	Lung cancer (162)	*PEMFs* < Median > Median ≥ 90th percentile First exposed 0–20 yr before diagnosis: < Median > Median ≥ 90th percentile First exposed > 20 yr before diagnosis: < Median > Median ≥ 90th percentile	 200 308 84 198 273 67 78 128 27	OR 1.00 1.27 (0.96–1.68) 3.11 (1.60–6.04) 1.00 1.48 (1.08–2.03) 1.80 (1.13–4.30) 1.00 3.83 (1.45–10.10) 7.02 (1.77–27.87)	SES	Nested case–control analysis Controls for each case were selected at random from the cases risk set and matched to the case by utility and year of birth. Exposure was counted only up to the date of diagnosis of the case.
Szmigielski (1996) Poland	Average of 127 800 men, yearly during 15 yr	1971–85	Military safety (health and hygiene) groups classified military service posts as having exposure, or not, to RF	Cancer of the larynx and lung	*Occupational exposure to RF* Not exposed Exposed	 [420]* [13]*	*Incidence rate ratios* 1.00 1.06 (0.72–1.56)	None specified	Cross-sectional study.
Tynes *et al.* (1996) Norway	2619 women	1961–91	Radio and telegraph operators with potential exposure to RF and ELF fields	Lung (ICD-7 code 162) Breast (ICD-7 code 170) Uterus (ICD-7 code 172)	*Potential exposure* Lung Breast Uterus	 5 50 12	*SIR* 1.2 (0.4–2.7) 1.5 (1.1–2.0) 1.9 (1.0–3.2)	Age, time since certification, calendar year, age at first childbirth	Women certified as radio and telegraph operators 1920–80

Table 2.6 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Lagorio *et al.* (1997) Italy	481 women	1962–92	Occupational history from plant records. RF generated by dielectric heat sealers. Exposure of 10 W/m^2 equivalent power-density frequently exceeded.	Lung (162)	*Job title*		*SMR*	Sex, age, calendar period-specific regional person-yr at risk	Mortality analysis; restricted to women
					RF-sealer operators	1	[5 (1.27–27.85)]*		
					Other workers	0	-		
					All female workers	1	[3.3]*		
Morgan *et al.* (2000) USA	195 775	1976–96	Job-exposure matrix, developed through expert consultation that categorized each of 9724 job titles into different RF exposure groups: background, low, moderate, and high, corresponding roughly to < 0.6 W, 0.6 to < 2.0 W, 2.0 to < 5.0 W, 5.0 to < 50 W and ≥ 50 W, respectively.	Respiratory system cancer	*RF exposure*		*SMR*	Age, sex, and race for external comparisons; and age, sex, and period of hire for internal comparisons	All employees of Motorola; exposure from cellular phones not assessed. Definition of exposure categories unclear
					High and moderate	94	[approx. 0.8]*		

Table 2.6 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Groves *et al.* (2002) USA	40 581 men (271 women excluded)	1950–97	United States Navy personnel with potential for RF exposure; job classified as having low or high exposure by a consensus of Navy personnel involved in training and operation	Trachea, bronchus and lung (162)	*Job-associated exposure to RF* Low High	 497 400	*SMR* 0.87 (0.79–0.94) 0.64 (0.58–0.70)	Age at cohort entry and attained age	White United States Navy (male) veterans of Korean War (1950–54) Reference: all white men, USA
Degrave *et al.* (2009) Belgium	Military personnel (4417 men) in batallions equipped with radar, and 2932 controls.	1968–2003	Exposure levels on the site where the battalion lived and worked were characterized; individual exposure assessment could not be conducted.	Respiratory and intra-thoracic organs (160–169)	Control cohort Radar exposed	28 45	1.00 1.07 (0.66–1.71)		Cause of death found for 71% of the men in the radar group and 70% in the control group.

* Values calculated/deduced by the Working Group

ELF, extremely low frequency electric and magnetic field; MW, microwaves; OR, odds ratio; PEMFs, pulsed electromagnetic fields; RF, radiofrequency radiation; SES, socioeconomic status; SIR, standardized incidence ratio; SMR, standardized mortality ratio; W, watt; V, volt; wk, week; yr, year

Hocking *et al.* (1996) studied incidence and mortality attributable to cancer of the brain (ICD-9 code 191) near three television and FM-radio broadcasting antennae located close together in Sydney, Australia. Exposure from these towers was to amplitude modulation (AM) at 100 kW and frequency modulation (FM) at 10 kW for signals at 63–215 MHz. Calculated power densities of RF radiation ranged from 8.0 μW/cm^2 near the tower to 0.2 μW/cm^2 at a distance of 4 km and 0.02 μW/cm^2 at 12 km. For cancer of the brain at all ages in three "inner ring" municipalities relative to six "outer-ring" municipalities, the rate ratio for incidence was 0.89 (95% CI, 0.71–1.11; 740 cases) and the rate ratio for mortality was 0.82 (95% CI, 0.63–1.07; 606 deaths). [Municipality-specific incidence rates were only available in broad, sex-specific age groups: 0–14, 15–69 and ≥ 70 years]. For children aged 0–14 years, the corresponding rate ratios were 1.10 (95% CI, 0.59–2.06; 64 cases) and 0.73 (95% CI, 0.26–2.10; 30 deaths). All municipalities were said to have upper middle-class populations.

Prompted by reported clustering of leukaemia and lymphoma near a high-power television and FM-radio broadcast antenna in the West Midlands, England, Dolk *et al.* (1997a) studied the incidence of cancer within a radius of 10 km from the antenna. The authors noted that available field-strength measurements generally showed a decrease of the average field strength with increasing distance from the transmitter, although with undulations in predicted field strength up to about 6 km from the transmitter. The maximum total power-density equivalent summed across frequencies at any one measurement point was 0.013 W/m^2 for television, and 0.057 W/m^2 for FM radio. Observed numbers of cases within 0–2 km and 0–10 km of the antenna were compared with "national" incidence rates, adjusted for age, sex, year and deprivation quintile (calculated based on data on unemployment, overcrowding, and social class of head of household). For all tumours of the brain (ICD-8/ICD-9 codes 191, 192, 225, and ICD-9 codes 237.5, 237.6, 237.9) in persons aged ≥ 15 years, the SIR was 1.29 (95% CI, 0.80–2.06) within 0–2 km and 1.04 (95% CI, 0.94–1.16) within 0–10 km. For malignant tumours of the brain only, these SIRs were 1.31 (95% CI, 0.75–2.29) and 0.98 (95% CI, 0.86–1.11), respectively.

Dolk *et al.* (1997b) undertook a similar analysis of cancer incidence in proximity to all 20 other high-power radio and television transmitter antennae in the United Kingdom. [With one exception, information about field distribution and strength in proximity to those antennae was not provided.] In this analysis, results for tumours of the brain were reported only for children aged 0–14 years and in proximity to all 21 such antennae (including that studied by Dolk *et al.*, 1997a). At 0–2 km from the antenna, SIRs were 0.62 (95% CI, 0.17–1.59) for all tumours of the brain and 0.50 (95% CI, 0.10–1.46) for malignant tumours, while at 0–10 km SIRs were 1.06 (95% CI, 0.93–1.20) and 1.03 (95% CI, 0.90–1.18), respectively.

Ha *et al.* (2003) studied the incidence of cancer between November 1993 and October 1996 in people aged ≥ 10 years in populations of 11 administrative areas of the Republic of Korea within about 2 km of high-power (≥ 100 kW) AM transmitter antennae, 31 such areas within about 2 km of low-power AM transmitter antennae (50 kW), and 4 control areas near, but not within 2 km, of each high-power transmitter antenna (44 control areas in total). Incident cases of cancer were ascertained from medical insurance records [no information was given regarding the completeness and accuracy of these records]. Directly age-standardized incidence rate ratios for cancer of the brain (ICD-9 codes 191–192, and ICD-10 codes C70–C72) comparing people living near high-power transmitter antennae with people living near low-power antennae were 1.8 (0.9–11.1) in males and females combined. Indirectly age-standardized incidence rate

ratios for cancer of the brain comparing people living near high-power transmitter antennae at different levels of power output with those in control areas were 2.27 (95% CI, 1.30–3.67) for a power output of 100 kW, 0.86 (95% CI, 0.41–1.59) for 250 kW, 1.47 (95% CI, 0.84–2.38) for 500 kW, and 2.19 (95% CI, 0.45–6.39) for 1500 kW.

Park *et al.* (2004) reported the results of a similar study of cancer mortality in 1994–95 in people of all ages in the Republic of Korea. Mortality rates within an area of 2 km surrounding AM broadcasting towers with a power of > 100 kW were compared with those in control areas that had a similar population and were located in the same province as the matched exposed area. Information on deaths due to cancer was identified in Korean death certificates from 1994 to 1995. The resident population at that time was assumed to correspond to that recorded in the nationwide population census of 1990. To control for possible selection bias, four control areas (n = 40) were matched to each exposed area (n = 10). Based on six age groups, annual age-adjusted world population-standardized mortality rates were calculated per 100 000 residents. Mortality rate ratios (MRR) were calculated comparing 10 areas within about 2 km of high-power antennae with 40 areas situated > 2 km from high-power antennae in the same or neighbouring provinces. The directly standardized MRR for cancer of the CNS, comparing areas near high-power antennae with control areas, was 1.52 (95% CI, 0.61–3.75).

The incidence of cancer in relation to mobile-phone base-station coverage was investigated in 177 428 people living in 48 municipalities in Bavaria, Germany, between 2002 and 2003 (Meyer *et al.*, 2006). Municipalities were classified on a crude three-level exposure scale based on the operating duration of each base station and the proportion of the population living within 400 m of the base station. Based on 1116 malignant tumours in 242 508 person–years, no indication of an overall increase in the incidence of cancer was found in the populations of municipalities belonging to the highest exposure class. The Potthoff-Whittinghill test was used to examine the homogeneity of the case distribution among the communities. The following cancers were not found to be heterogeneously distributed: breast (P = 0.08); brain and CNS (P = 0.17); and thyroid (P = 0.11). For leukaemia, there were indications of underreporting and thus the test for homogeneity was not performed. [The exposure assessment in this study was very crude and likely to result in substantial random exposure misclassification. The number of organ-specific tumours was not reported, but is expected to be small given the total number of tumours. Thus, the observed absence of an association may be real, or due exposure misclassification, or to inadequate statistical power.]

(b) Case–control studies

Schüz *et al.* (2006b) reported on the association of proximity of a DECT (Digital Enhanced Cordless Telecommunications) cordless-phone base station to a person's bed (a proxy for continuous low-level exposure to RF radiation during the night) with the risk of brain glioma and mengioma in a case–control study in Germany that was a component of the INTERPHONE study. This was a subanalysis of the main study in which no association of either brain glioma or meningioma with use of cordless phones had been found (Schüz *et al.*, 2006a). Cases were newly diagnosed with a histologically confirmed glioma or meningioma in 2000–03, aged 30–69 years, lived in the study region, had a main residence in the study region, and had a knowledge of German sufficient for interview. Proxy interviews were conducted if the cases or controls had died or were too ill for interview. Controls were selected randomly from compulsory population registers in the study regions, were required to meet relevant case-inclusion criteria, and were initially frequency-matched to the cases by age, sex and region. Participation rates were: patients

with glioma, 79.6%; patients with meningioma, 88.4%; and controls, 62.7%. Interview questions about cordless phones addressed the type of phone (DECT or analogue), make and model, the dates on which use started and stopped, and the location of the base station within the residence. Since many subjects could not recall whether their cordless phone was a DECT phone, information on the make, model and price of the phone and its technical features were used to classify phones into "definitely" or "possibly" DECT, or definitely analogue. Participants were considered definitely or possibly exposed if, in addition, the DECT base station was located 3 m or less from the bed (this was the case for 1.6% of participants). Information from proxy interviews (patients with glioma, 10.9%; patients with meningioma, 1.3%; and control participants, 0.4%) was used in the analysis, since most proxies lived with their index subjects and were users of the same cordless phones. For analysis, controls were individually matched 2 : 1 to cases by birth year, sex, region and date of diagnosis (case) or interview (control); 366 cases of glioma and 381 cases of meningioma were analysed. Risk of glioma or meningioma was not increased with definite or possible exposure to DECT base stations; nor was there any consistent trend with time since first exposure (Table 2.7). [This study was limited by the small proportion of people who were considered to be exposed, difficulty in classifying cordless phones as DECT or analogue, and lack of associated consideration of other sources of exposure to RF radiation.]

Ha *et al.* (2007) reported on risk of childhood cancers of the brain in relation to residential exposure to RF radiation from AM-radio fixed-site transmitters (power, > 20 kW) in the Republic of Korea. Cases were diagnosed with cancer of the brain (ICD-9 codes 191–192, and ICD-10 codes C70–C72) between 1993 and 1999, and controls were diagnosed over the same period with a respiratory disease (ICD-9 codes 469–519, and ICD-10 codes J20 and J40–J46). Both cases and controls were identified through the national health insurance system of the Republic of Korea, and individually matched by age, sex and year of first diagnosis. Both were restricted to children diagnosed at one of fourteen large cancer or tertiary-care hospitals. Cancer diagnoses were confirmed by reference to the national cancer registry or hospital medical records [the basis for confirmation was not stated]. Cases were excluded if the diagnosis of cancer could not be confirmed; controls were excluded if they had a history of cancer recorded in the national cancer registry (which was 80% complete in 1998); and both were excluded if they had incomplete addresses (which were obtained from the medical records). The distance from each subject's residence to the nearest AM-radio transmitter established before diagnosis was evaluated by means of a geographical information system, and total exposure to RF radiation from all AM-radio fixed-site transmitters was estimated with a flat-earth attenuation statistical-prediction model, which took into account features of the receiving point and the propagating pathway [intervening terrain, the output power of the fixed-site transmitters and their distance from the receiving point]. The prediction program was validated by taking measurements of field strength at sites around 11 fixed-site transmitters, and correction coefficients were calculated and applied to the prediction program. Twenty-nine of the thirty-one radio fixed-site transmitters were established between 1980 and 1995, and children in the study were born between 1978 and 1999. Socioeconomic status was classified according to the number of cars owned per 100 people in defined regions and population density in these regions was used as a surrogate for industrialization and environmental pollution. The odds ratio for cancer of the brain was not materially increased in those living closest (≤ 2 km) to a transmitter (OR, 1.42; 95% CI, 0.38–5.28) or in those with greatest estimated exposure (≥ 881 mV/m) to RF radiation (OR, 0.77; 95% CI, 0.54–1.10) (Table 2.7). [This

Table 2.7 Case–control studies of cancer of the brain and environmental exposure to radiation from transmitters of radiofrequency signals

Reference, study location and period	Total cases	Total controls	Control source (hospital, Population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Comments
Schüz *et al.* (2006b) Bielefeld, Heidelberg, Mainz, Mannheim, Germany, 2000–03	747	1494	Population	Interviewer-administered questionnaire	Brain (glioma and meningioma)	*DECT cordless-phone base station ≤ 3m from bed*			Covariates: age, sex, region, educational level
						Glioma			
						Definitely			
						No	342	1.00	
						Yes	3	0.50 (0.14–1.76)	
						Possibly or definitely			
						No	342	1.00	
						Yes	5	0.82 (0.29–2.33)	
						Time since first exposure (possibly or definitely)			
						No, < 1 yr	342	1.00	
						1–4 yr	3	0.95 (0.24–3.70)	
						≥ 5 yr	2	0.68 (0.14–3.40)	
						Meningioma			
						Definitely			
						No	360	1.00	
						Yes	5	1.09 (0.37–3.23)	
						Possibly or definitely			
						No	364	1.00	
						Yes	5	0.83 (0.29–2.36)	
						Time since first exposure (possibly or definitely)			
						No, < 1 yr	364	1.00	
						1–4 yr	1	0.33 (0.04–2.80)	
						≥ 5 yr	4	1.29 (0.37–4.48)	

Table 2.7 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, Population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Comments
Ha *et al.* (2007) Republic of Korea, 1993–99	956	1020	Hospital-based study. Controls had attended one of 14 large cancer or tertiary care hospitals where the cases had been diagnosed, for management of respiratory disease (ICD-9 469–519; ICD-10 J20 and J40–46). Controls were individually matched to a case by age, sex, and year of first diagnosis.	Based on locations of 31 AM transmitters of ≥ 20 kW and 49 associated antennae and locations of subjects' residences at time of diagnosis.	Brain (ICD-9 code 191–192; ICD-10 codes C70–C72)	*Distance from nearest AM radio-transmitter established before subject's year of diagnosis (km)*	All brain cancer (age < 15 yr)		Children aged < 15 yr. The use only of large hospitals for ascertainment of controls could mean that controls are not representative of population from which cases were drawn. Covariates: age, sex, residential location, population density, SES
						≤ 2	10	1.42 (0.38–5.28)	
						> 2–4	32	1.40 (0.77–2.56)	
						> 4–6	59	1.02 (0.66–1.57)	
						> 6–8	90	1.08 (0.73–1.59)	
						> 8–10	114	0.94 (0.67–1.33)	
						> 10–20	244	1.01 (0.77–1.34)	
						> 20	400	1.00 (reference)	
						Unknown	7	4.30 (0.50–36.73)	
						P (trend)		0.76	
						Total exposure to RF (mV/m)			
						< 532.55*	329	1.00 (reference)	*Quartiles of the distribution
						532.55 – < 622.91	185	0.66 (0.47–0.92)	
						622.91 – < 881.07	181	0.72 (0.51–1.01)	
						≥ 881.07	254	0.77 (0.54–1.10)	
						P (trend)		0.73	

Table 2.7 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, Population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Comments
Ha *et al.* (2007) (cont.)						*Distance from nearest AM radio-transmitter established before subject's year of diagnosis (km)*	All brain cancer (age < 1 yr)		
						≤ 10	10	0.41 (0.05–3.10)	
						> 10–20	10	0.49 (0.06–3.80)	
						> 20	12	1.00 (reference)	
						P (trend)		0.78	
						Total exposure to RF (mV/m)			
						< 485.85*	9	1.00 (ref.)	
						485.85 – < 632.96	7	3.56 (0.49–25.95)	
						632.96 – < 810.81	7	1.41 (0.12–17.11)	
						≥ 810.81	9	5.13 (0.44–60.26)	
						P (trend)		0.27	
Oberfeld (2008) Hausmannstätten & Vasoldsberg, Austria, 1984–97									The status of this study (printed version, German and English online versions) is controversial. It was therefore decided to remove the description of this study from text and tables.

Table 2.7 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, Population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Comments
Spinelli *et al.* (2010) Western Provence-Alpes-Côte d'Azur (PACA), France, 2005	122	122	Hospital-based	Self-administered questionnaire and face-to-face interview, including lifetime job history, job title, dates, tasks	Brain (glioma grades II–IV)	*Residence within 500 m of:*			Covariates: age, sex
						Cell-phone tower	19	0.49 (0.26–0.92)	
Elliott *et al.* (2010) United Kingdom, 1999–2001	251	1004	Population-based study. Controls were children aged < 4 yr, individually matched to cases by sex and date of birth.	Location of birth residence relative to nearby macro-cell mobile-phone base stations; distance to nearest base station; total power output of all base-stations within 700 m; modelled power density at birth address	Brain and CNS (ICD-10 codes C71–C72)	*Distance from nearest macro-cell mobile-phone base-station*			Covariates: percentage of population with education to degree level or higher, Carstairs score (a composite area-deprivation measure), population density, and population mixing (percentage immigration into the area over the previous year).
						Lowest third	85	1.00	
						Intermediate third	85	0.95 (0.67–1.34)	
						Highest third	81	0.95 (0.65–1.38)	
						For 15th to 85th centile increase (continuous measure)	251	1.12 (0.91–1.39)	
						Total mobile-phone frequency power-output (kW)			
						No base station within 700 m	150	1.00	
						Lower half	56	1.02 (0.72–1.46)	
						Upper half	45	0.83 (0.54–1.25)	
						For 15th to 85th centile increase (continuous measure)	251	0.89 (0.73–1.09)	

Table 2.7 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, Population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Comments
Elliott *et al.* (2010) (contd.)						*Modelled mobile-phone frequency power density (dBm)*			
						Lowest third	93	1.00	
						Intermediate third	80	0.97 (0.69–1.37)	
						Highest third	78	0.76 (0.51–1.12)	
						For 15th to 85th centile increase (continuous measure)	251	0.82 (0.55–1.22)	

AM, amplitude modulation (radio); CNS, central nervous system; DECT, Digital Enhanced Cordless Telecommunications; kW, kilowatt; NMT, Nordic Mobile Telephone (standard); RF, radiofrequency radiation; SES, socioeconomic status; yr, year

study was limited by the lack of a clear population base, possible mismatch between the population sampled for cases and that sampled for controls, and the lack of a cumulative measure of exposure to RF radiation that took into account variation in an individual's place of residence between birth and diagnosis of cancer or respiratory disease.]

[Oberfeld (2008): the status of this study (printed version, German and English online versions) is controversial. It was therefore decided to remove the description of this study from text and tables.]

Spinelli *et al.* (2010) undertook a pilot case–control study of newly diagnosed, histopathologically confirmed malignant primary tumours of the brain (defined as previously untreated glioma, grades II–IV) in people aged ≥ 18 years treated in the two principal referral hospitals for cancer of the brain in the west of the Provence-Alpes-Côte d'Azur (PACA) region in France. Controls were other patients in the neurosurgery department who were hospitalized for reasons other than cancer (mainly herniated intervertebral disc, intracranial aneurysm, trauma, and epidural haematoma) who were individually matched to cases by age, sex and residence in the west of PACA. Participants completed a self-administered questionnaire and were interviewed by an occupational physician at the hospital they attended within 3 months after surgery; the physician also checked their questionnaire. [It was not stated whether the interviewer was blind to the case or control status of participants.] Family members also helped with self-administered questionnaires, more often for cases than controls. Proxy interviews were completed for 2% of cases. Occupational exposures were the principal focus of the questionnaire and interview, but participants were also asked about use of mobile phones and residence in proximity to a mobile-phone tower. Information was obtained from 75.3% of cases [the participation rate of controls was not stated]. Nineteen cases and thirty-three controls reported a mobile-phone tower within 500 m of their residence (age- and sex-adjusted OR, 0.49; 95% CI, 0.26–0.92) (Table 2.7). [This study was limited by its small size and because it was hospital-based. The participation rate for controls was not stated and it is likely that people prone to serious injury were over-represented among the controls. The interviewer may not have been blind to the case or control status of participants. Specific questions regarding proximity of residence to mobile-phone towers were not described and may have been highly prone to recall error, and there were few participants with occupational exposure to RF radiation.]

Elliott *et al.* (2010) undertook a case–control study of early childhood cancer in the United Kingdom based on all cases of cancer in children aged 0–4 years registered in 1999–2001. Of 1926 registered cases, the geographical coordinates of addresses at birth, and exposure based on the birth address were available for 1397 children (73%). Of the latter, 251 had cancers of the brain and CNS (ICD-10 codes C71–C72). For each case, four controls from the national birth register, with complete birth addresses and individually matched to cases by sex and date of birth (5588 controls), were obtained from 6222 originally randomly selected (90%). The four national mobile-phone operators provided detailed data on all 76 890 macro-cell base stations operating in 1996–2001. Three exposure measures for the birth address of each case and control were obtained: the distance from the nearest macro-cell mobile-phone station; the total power output (kW) from summation across all base stations within 700 m; and computed modelled power density (dBm) at each birth address for base stations within 1400 m. Exposures beyond 1400 m were considered to be at background levels. Measurements from field campaigns in a rural and an urban area were used to set parameter values in the power-density model. The models were validated with data from two further surveys and power-density measurements from 620 locations

across the country. Spearman's correlation coefficients between measured power density and the exposure measures were: 0.66 with modelled power density, 0.72 with distance from nearest base station, and 0.66 with total power output. The exposure measures estimated at each birth address were averaged across monthly estimates for the assumed 9 months of the pregnancy in each case. Each exposure measure was divided into thirds of the distribution across all cases and controls except for total power output, which was zero for 58% (no base station within 700 m), with the remaining 42% in two halves of their distribution. Exposure measures were fitted to models as continuous variables as well as in the above categories. Neither unadjusted nor partly or fully adjusted odds ratios suggested that risk of childhood cancer of the brain increased with increasing exposure to RF radiation from nearby macro-cell mobile-phone base stations (Table 2.7). [This study was limited by the fact that estimation of exposure was confined to the gestational period; application of birth address to the whole of gestation was assumed; and ecologically measured possible confounding variables were used to apply to individual subjects.]

(c) Cohort studies

No data were available to the Working Group.

2.2.2 Leukaemia and lymphoma

(a) Ecological studies

See Table 2.8

Hocking *et al.* (1996) published a study comparing incidence of and mortality from leukaemia during 1972–90 in nine municipalities, three of which were located around television towers and six that were more distant. Increased rate ratios for incidence (IRR, 1.24; 95% CI, 1.09–1.40) and mortality (MRR, 1.17; 95% CI, 0.96–1.43) for leukaemia at all ages were obtained and generally higher rate ratios were seen for childhood leukaemia (IRR, 1.58; 95% CI, 1.07–2.34; MRR, 2.32; 95% CI, 1.35–4.01) than for leukaemia at all ages, comparing the three "inner ring" municipalities with six "outer ring" municipalities. A more marked association was observed between proximity to television towers and mortality (MRR, 2.4; 95% CI, 1.4–3.7) than incidence (IRR, 1.8; 95% CI, 1.2–2.5) from leukaemia. [No individual measurements were undertaken and main analyses could only be adjusted for covariates by group-level (aggregated) data.]

In 1997, Dolk *et al.* published two studies on cancer incidence during 1974–86. The first was a study in a small area in response to an unconfirmed report of a cluster of leukaemias and lymphomas near the Sutton Coldfield television and radio-transmitter in the West Midlands, England (Dolk *et al.*, 1997a). The second, to place in context the findings of the Sutton Coldfield study, was carried out near 20 high-power television and radio-transmitters in the United Kingdom (Dolk *et al.*, 1997b). In the Sutton Coldfield study, an increased risk of leukaemia in adults was found when the observed and expected numbers of cases (derived from national incidence rates) were compared (observed/expected, 1.83; 95% CI, 1.22–2.74) within 2 km of the transmitter and there was a decline in risk with distance (Stone's P value = 0.001). The latter was tested by use of 10 bands of increasing distance from the transmitter within a circle with a radius of 10 km around it. The findings appeared to be consistent between 1974 and 1980, and 1981 and 1986. For NHL, a suggestion of a decrease in risk was seen within the 2 km area (observed/expected, 0.66; 95% CI, 0.28–1.30) while for the total study area of 0–10 km, risk appeared to be increased (observed/expected, 1.23; 95% CI, 1.11–1.36). In the second study, covering the United Kingdom (Dolk *et al.*, 1997b), evidence of a decline in risk of leukaemia was found with increasing distance from the transmitter (Stone's P value = 0.05); however, the magnitude (at 0–10 km: observed/expected, 1.03; 95% CI, 1.00–1.07) and the pattern

Table 2.8 Ecological studies of leukaemia and lymphoma and environmental exposure to radiation from transmitters of radiofrequency signals

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Hocking *et al.* (1996) Australia	585 000	1972–90	Residential proximity to TV towers	Leukaemia (204–208)	Overall rate ratios for incidence and mortality, respectively, inner and outer residential area compared.	1206/847	Incidence, 1.24 (1.09–1.40) Mortality, 1.17 (0.96–1.43)	Age, sex, calendar period	Reference population: whole of New South Wales
					Inner area *vs* ref. population	33	Childhood SIR, 1.8 (1.2–2.5)		
					Outer area *vs* ref. population	101	Childhood SIR, 1.1 (0.9–1.4)		
					Inner area *vs* ref. population	19	Childhood SMR 2.4 (1.4–3.7)		
					Outer area *vs* ref. population	40	Childhood SMR 1.0 (0.7–1.4)		
Dolk *et al.* (1997a) United Kingdom	Around 408 000	1974–86	Distance to Sutton Coldfield radio and TV transmitter	Haemato-poietic and lymphatic cancers (200–202; 203 + 238.6; 204–208)	Distance 0–2 km Distance 0–10 km Stone's *P*-value	45 935	1.21 (0.91–1.62) 1.04 (0.98–1.11) Unconditional $P = 0.153$	Region	Observed/expected ratios and Stone's *P*-value are given for persons aged ≥ 15 yr, stratified by age, sex, year, and SES. Declining risk with increasing distance was seen only for all leukaemias.
				Leukaemia (204–208)	Distance 0–2 km Distance 0–10 km Stone's *P*-value	23 304	1.83 (1.22–2.74) 1.01 (0.90–1.13) Unconditional $P = 0.001$ Conditional $P = 0.001$		
				NHL	Distance 0–2 km Distance 0–10 km Stone's *P* value	8 357	0.66 (0.28–1.30) 1.23 (1.11–1.36) Unconditional $P = 0.005$ Conditional $P = 0.958$		

Table 2.8 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Dolk *et al.* (1997b) United Kingdom	Around 3 390 000	1974–86	Distance to radio and television transmitters in the United Kingdom (excluding Sutton Coldfield)	Leukaemia (204–208)	Distance 0–2 km Distance 0–10 km Stone's *P* value	79 3 305	0.97 (0.78–1.21) 1.03 (1.00–1.07) Unconditional *P* = 0.001 Conditional *P* = 0.052	Region	Observed/expected ratios and Stone's *P* value are given for persons aged ≥ 15 yr, stratified by age, sex, year, and SES.
Cooper *et al.* (2001) United Kingdom	NR	1987–94	Distance to Sutton Coldfield television transmitter	Leukaemia (204–208)	Distance from transmitter: 0–2 km, all ages, all persons 0–10 km, all ages, all persons Stone's *P* values, all ages, all persons 0–2 km, age 0–14 yr, all persons 0–10 km, age 0–14 yr, all persons Stone's *P* values, age 0–14 yr, all persons	 20 333 1 26 	 1.32 (0.81–2.05) 1.16 (1.04–1.29) Unconditional *P* = 0.038 Conditional *P* = 0.409 1.13 (0.03–6.27) 1.08 (0.71–1.59) Unconditional *P* = 0.420	-	Observed/expected ratios and Stone's *P* values (unconditional and conditional) are given. Stratified by age, sex, and social deprivation. Results for other haematopoietic cancers are reported in the manuscript.

Table 2.8 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Michelozzi *et al.* (2002) Italy	49 656	1987–99	Distance to Vatican radio station, Rome	Leukaemia (204–208)	Distance from radio station (km), (cumulative areas)			Deprivation index	
					Total (age > 14 yr)		*SMR*		
					0–2	2	1.8 (0.3–5.5)		
					0–4	11	1.5 (0.8–2.6)		
					0–6	23	1.2 (0.8–1.8)		
					0–8	34	1.2 (0.8–1.6)		
					0–10	40	1.1 (0.8–1.4)		
					P, Stone's conditional test		0.14		
					Children (age 0–14 yr)		*SIR*		
					0–2	1	6.1 (0.4–27.5)		
					0–4	3	2.9 (0.7–7.6)		
					0–6	8	2.2 (1.0–4.1)		
					0–8	8	1.5 (0.7–2.7)		
					0–10	8	1.2 (0.6–2.3)		
					P, Stone's conditional test		0.036		

Table 2.8 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Ha *et al.* (2003) Republic of Korea	From 3 152 to 126 523 persons per area (total not given)	1993–96	Distance ≤ 2 km from AM transmitter	Leukaemia (204–208)	*High-power (≥ 100 kW) vs low-power (50 kW) transmitter sites:*		*Rate ratio*	Age	Rate ratios (RR) and observed/expected (O/E) ratios are given For all cancers combined: RR, 1.2 (95% CI, 1.1–1.4) for high- *vs* low-power transmitters
					Men	8.3/6.8 per 100 000 person-yr	1.2 (0.5–5.3)		
					Women	8.7/4.6 per 100 000 person-yr	1.9 (0.8–8.7)		
					Total	8.5/5.7 per 100 000 person-yr	1.5 (0.7–6.6)		
					Transmitter power of sites:		*O/E*		
					100 kW	9	1.20 (0.55–2.28)		
					250 kW	12	2.45 (1.27–4.29)		
					500 kW	10	0.65 (0.31–1.19)		
					1500 kW	4	4.26 (1.16–10.89)		

Table 2.8 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Ha *et al.* (2003) (contd.)				Malignant lymphoma (200–202)	*High-power (≥ 100 kW) vs low-power (50 kW) transmitter sites:*		*Rate ratio*		
					Men	10.5/7.1 per 100 000 person-year	1.5 (0.7–8.6)		
					Women	8.7/7.1 per 100 000 person-year	1.2 (0.6–5.6)		
					Total	9.6/7.1 per 100 000 person-year	1.4 (0.6–7.0)		
					Transmitting power of sites:		*O/E*		
					100 kW	9	1.10 (0.51–2.10)		
					250 kW	13	1.28 (0.68–2.19)		
					500 kW	16	0.98 (0.56–1.59)		
					1 500 kW	1	0.44 (0.01–2.48)		

Table 2.8 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Park *et al.* (2004) Republic of Korea	8 115 906 (of whom 1 234 123 in exposed area)	1994–95	Regions including AM-radio broadcasting towers of > 100 kW	Leukaemia (ICD-10 codes C90–95), including multiple myeloma	Total exposed *vs* control (unexposed)	55	1.70 (0.84–3.45)	Age	Direct standardized MRRs are given
					Males	33	1.89 (0.75–4.75)		
					Females	22	1.55 (0.52–4.68)		
					Age (yr)				
					0–14	11	2.29 (1.05–5.98)		
					15–29	11	2.44 (1.07–5.24)		
					30–44	9	2.16 (0.95–4.04)		
					45–59	5	0.73 (0.48–2.89)		
					60–74	10	0.87 (0.57–2.78)		
					≥ 75	6	3.08 (0.95–6.59)		
				Malignant lymphoma (ICD-10 codes C81–88)	Total exposed *vs* control (unexposed)	31	1.60 (0.72–3.56)		
					Males	19	1.52 (0.56–4.14)		
					Females	12	1.80 (0.48–6.71)		
					Age (yr)				
					0–14	1	2.46 (0.07–82.66)		
					15–29	2	1.51 (0.15–15.18)		
					30–44	5	1.94 (0.37–10.20)		
					45–59	8	1.76 (0.43–7.15)		
					60–74	13	1.41 (0.47–4.14)		
					≥ 75	2	0.55 (0.05–5.67)		

AM, amplitude modulation (radio); kW, kilowatt; MRR, mortality rate ratio; NR, not reported; O/E, observed/expected; SIR, standardized incidence ratio; SMR, standardized mortality ratio; TV, television; *vs*, versus; yr, year

of risk seen in the Sutton Coldfield study could not be replicated. Most notably, in the second, nationwide study no increase in risk was seen nearest (within 2 km) the transmitters.

In a letter to the editor, Cooper *et al.* (2001) published updated results on adult and childhood leukaemia (1987–94) near the Sutton Coldfield transmitter. To investigate risk according to distance, the authors defined the study area as a series of 10 concentric circles around the Sutton mast and calculated the expected number of cases (by numbers, child/adult and sex) for each of the circles and for different cancer sites. Most results for childhood cancers gave no evidence of a decline in the ratios of observed-to-expected numbers of cases with distance from the transmitter. There was some support for a decline in risk of childhood leukaemia in males, as indicated by Stone's test. The risk also declined for acute myeloid leukaemia in adult females, for all leukaemias (females and all persons separately), and for haematopoietic and lymphatic cancers in females. The same four groups were at higher risks over the whole study area (0–10 km). An increased risk was found for acute lymphatic leukaemia within 2 km of the transmitter; however this was based on only two cases. Elevated risks were found for leukaemias and NHL (males and females combined and separately) over the whole study area. No increase or decrease in the ratios of observed-to-expected numbers of cases was seen for NHL.

Michelozzi *et al.* (2002) published a study on incidence and mortality for adult and childhood leukaemia in an area of 10 km around a high-power radio station in Rome. This station had numerous transmitters with different transmission powers (5–600 kW) operating at different frequencies (short–medium wave). An increased incidence of childhood leukaemia (SIR, 2.2; 95% CI, 1.0–4.1) was found up to 6 km from the radio station; there was a decline with increasing distance from the station for mortality in males and for incidence from childhood leukaemia. [The small number of cases, possible unmeasured confounding and lack of individual or calculated exposure assessment were some limitations of the study.]

Ha *et al.* (2003) published a study on the incidence of cancer in the Republic of Korea in 1993–96 in areas proximate to 42 AM-radio-transmitters, characterized by transmission power. An increased rate ratio comparing sites exposed to high-power versus low-power transmitters was seen for all cancers combined (rate ratio, 1.2; 95% CI, 1.1–1.4), while confidence intervals by cancer type were wide, e.g. for leukaemia (rate ratio, 1.5; 95% CI, 0.7–6.6) and malignant lymphoma (rate ratio, 1.4; 95% CI, 0.6–7.0). However, at two of eleven high-power sites, more pronounced increases in the incidence of leukaemia were found. [Interpretation was hampered by limitations related to the ecological design, study size, exposure and outcome assessment, and lack of controls for confounding. There was partial overlap in the populations included in Park *et al.* (2004) and Ha *et al.* (2007).

Park *et al.* (2004) published a study that evaluated cancer mortality in the Republic of Korea in relation to exposure to AM-radio-transmitters. Mortality from leukaemia was higher in exposed areas than in control areas (standardized mortality rate ratio, MRR, 1.70; 95% CI, 0.84–3.45), particularly among young adults (MRR, 2.44; 95% CI, 1.07–5.24), but also in children (MMR, 2.29; 95% CI, 1.05–5.98). According to the authors, however, there was no increasing or decreasing trend with respect to broadcasting power. [In this study, exposure assessment was poor (no individual data) and it was also unclear to what extent the mortality records reflected the true address of the subject, which was used as a proxy for exposure. Other limitations were the lack of control for confounding by socio-economic status, and possible non-differential disease misclassification.]

(b) Case–control studies

See Table 2.9

Maskarinec *et al.* (1994) published the results of a small case–control study that indicated an increased incidence in childhood leukaemia (SIR, 2.09; 95% CI, 1.08–3.65) near radio towers in Hawaii, USA. The SIR for acute lymphocytic leukaemia was 1.58 (95% CI, 0.63–3.26) and for acute non-lymphocytic leukaemia it was 3.75 (95% CI, 1.20–8.71). Seven cases of leukaemia had been reported during 1982–84, including all five cases of acute non-lymphocytic leukaemia (SIR, 5.34; 95% CI, 2.14–11.0) that were unusual with respect to sex, age, and type of leukaemia. Twelve cases in children aged < 15 years diagnosed with acute leukaemia in 1979–90 and residing in certain census tracts before diagnosis were included in the case–control study, along with 48 (80%) sex- and age-matched controls that lived in the same area at the time of diagnosis. Collection of data was by non-blinded telephone interviews with parents, which included questions on pregnancy, address, and residence history, the child's medical history and exposure of various kinds, including X-rays and smoking. In addition, the occupational history of both parents was recorded, together with potentially relevant exposures. The odds ratio for acute leukaemia among those having lived within 2.6 miles (4.2 km) of the radio towers before diagnosis was increased (OR, 2.0; 95% CI, 0.6–8.3). [The limitations of this study, besides poor assessment of exposure, were its low power to detect an effect (~50% for OR = 5) and the apparent lack of controls for confounding by socioeconomic status.]

Ha *et al.* (2007, 2008) published the results of a case–control study that was large enough to give moderate statistical power for detecting an effect of exposure to RF radiation on the risk of childhood leukaemia. Patients aged < 15 years with leukaemia and controls with respiratory illnesses were selected from 14 hospitals in the Republic of Korea and matched on age, sex and year of diagnosis (1993–99). From a total of 1928 cases of leukaemia and matched controls, risks were estimated by means of conditional logistic regression analysis adjusted for residential area, socioeconomic status and community population density. An increased risk of all types of leukaemia was found among children who lived within 2 km of the nearest AM-radio-transmitter (OR, 2.15; 95% CI, 1.00–4.67). For total exposure to RF radiation, most odds ratios decreased with predicted exposure. The authors reported an odds ratio of 1.40 (95% CI, 1.04–1.88) for lymphocytic leukaemia and 0.63 (95% CI, 0.41–0.97) for myelocytic leukaemia in the quartile of highest peak exposure, although no linear trend was evident with regard to the different exposure categories for total or peak exposure to RF radiation. [The main limitations of the study were related to the exposure estimates calculated by the prediction programme, e.g. the existence of buildings or irregular geographical features was not considered, nor was individual cumulative-exposure history assessed. There was partial overlap in the populations included in Ha *et al.* (2003) and Park *et al.* (2004).]

A case–control study on RF radiation and childhood leukaemia was conducted in west Germany by Merzenich *et al.* (2008). Cases (age, 0–14 years) diagnosed during 1984–2003 and registered at the German Childhood Cancer Registry were included, along with three age-, sex- and transmitter-area-matched controls per case that were drawn randomly from population registries. The analysis included 1959 cases and 5848 controls for which individual exposure to RF radiation 1 year before diagnosis was estimated by means of a field-strength prediction program. The study area encompassed municipalities in the vicinity of Germany's strongest transmitters, including 16 AM and 8 FM transmitters with a power of at least 20 kW. Conditional logistic regression analysis for all types of childhood leukaemia yielded no increase in odds ratio (OR,

Table 2.9 Case–control studies of leukaemia and lymphoma and environmental exposure to radiation from transmitters of radiofrequency signals

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comment
Maskarinec *et al.* (1994) Hawaii, USA, 1984–2003	12	48	Hospital	Having lived within 2.6 miles of low-frequency radio towers. Distances estimated both manually and by use of a geographical software package	Acute leukaemia (7 ALL, 5 ANLL)	Last residence before diagnosis within 2.6 miles [4.2 km] of radio towers.	8	2.0 (0.6–8.3)		Matched ORs are given; matching variables: age, sex
						Residence at birth within 2.6 miles of radio towers	8	2.2 (0.3–15)		
						Residence with the maximum number of years within 2.6 miles of radio towers	8	1.8 (0.5–6.3)		
Ha *et al.* (2007) Republic of Korea, 1993–99	1928	3082	Hospital	Prediction program incorporating a geographic information system	All leukaemia (204–208)	*Distance (km)*			Residential location, population density, SES	Conditional logistic regression; matching variables: age, sex, year of diagnosis. Cases aged < 15 yr. Corrected estimates for total RF exposure according to Ha *et al.* (2008)
						> 20	772	1.00		
						≤ 2	36	2.15 (1.00–4.67)		
						> 2–4	73	0.66 (0.44–0.99)		
						> 4–6	120	1.07 (0.77–1.49)		
						> 6–8	218	1.26 (0.96–1.65)		
						> 8–10	276	1.10 (0.85–1.41)		
						> 10–20	428	0.80 (0.65–0.99)		
						Unknown	5	0.48 (0.12–1.95)		
						P for trend		0.10		

Table 2.9 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comment
Ha *et al.* (2007) (contd.)						*Total exposure to RF (mV/m), quartiles (Q)*				In category Q4: OR for LL was 1.40 (95% CI, 1.04–1.88), and for ML, 0.63 (95% CI, 0.41–0.97)
						Q1	737	1.00		
						Q2	362	0.75 (0.58–0.97)		
						Q3	330	0.70 (0.55–0.90)		
						Q4	494	0.83 (0.63–1.08)		
						Unknown	5	0.39 (0.10–1.54)		
						P for trend		0.44		
Merzenich *et al.* (2008) Germany, 1984–2003	1959	5848	Population	Field-strength prediction programme	ICCC Ia, ICCC Ib, ICCC Ic, ICCC Id, ICCC Ie	*Quantiles of median exposure (V/m) to RF-EMFs (AM and FM/TV transmitter) one yr before diagnosis of case*				Conditional logistic regression; matching variables age, sex, year of diagnosis, study region. Cases were aged 0–14 yr.
						0 to < 90%	1772	1.00		
						90 to < 95%	101	1.02 (0.80–1.31)		
						95 to ≤ 100%	86	0.86 (0.67–1.11)		
						Distance (km), AM or FM/TV transmitter				
						10 to < 15	551	1.00		
						0 to < 2	25	1.04 (0.65–1.67)		
						2 to < 6	172	0.81 (0.66–0.99)		
						6 to < 10	314	0.79 (0.67–0.93)		
						≥ 15	866	1.00 (0.88–1.14)		

Table 2.9 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comment
Elliott *et al.* (2010) United Kingdom, 1999–2001	527	5588	Population	(a) Distance from nearest mobile phone base station; (b) Total power output from summation across all base stations within 700 m; (c) Modelled power density at each birth address for base stations within 1400 m	Leukaemia and NHL (C91–95, C82–85)	*Distance from nearest base station (m)*			Percentage of population with education to degree level or higher, Carstairs deprivation score, population density, population mixing	Conditional logistic regression; matching variables: age, sex. Cases aged 0–4 yr
						Lowest	182	1.00		
						Intermediate	167	0.99 (0.78–1.27)		
						Highest	178	1.05 (0.81–1.35)		
						P for trend		0.75		
						Total power output (kW)				
						Lowest	305	1.00		
						Intermediate	112	1.08 (0.84–1.38)		
						Highest	110	1.08 (0.80–1.42)		
						P for trend		0.58		
						Modelled power density (dBm)				
						Lowest	179	1.00		
						Intermediate	179	1.16 (0.90–1.48)		
						Highest	169	1.03 (0.79–1.34)		
						P for trend		0.51		

ALL, acute lymphocytic leukaemia; AM, amplitude modulation; ANLL, acute non-lymphocytic leukaemia; dBm, modelled power density; FM, frequency modulation; ICCC, International Classification of Childhood Cancer; kW, kilowatt; LL, lymphocytic leukaemia; ML, myelocytic leukaemia; OR, odds ratio; NHL, non-Hodgkin lymphoma; RF, radiofrequency radiation; SES, socioeconomic status; TV, television

0.86; 95% CI, 0.67–1.11) when the upper and lower quantiles of RF-radiation distribution were compared. In addition, there was no evidence for an association indicating increased or decreased risk by transmitter type or leukaemia subtype. Nor was there any increased risk (OR, 1.04; 95% CI, 0.65–1.67) for children residing within 2 km of the nearest transmitter. [Lack of information on peak and indoor exposure to RF radiation as well as cumulative lifetime exposure to RF radiation from transmitters, and the low number of cases residing within 2 km of the nearest AM transmitters were the main limitations of this study.]

A case–control study by Elliott *et al.* (2010) (described in Section 2.2.1) examined risk of childhood cancers (e.g. leukaemia and NHL) in association with maternal exposure to RF radiation from mobile-phone base stations during pregnancy. No association or trend for different exposure categories was found for leukaemia or NHL with any of the exposure metrics used. Sociodemographic measures as well as mean distance of birth address from nearest FM, television, and very high frequency (VHF) broadcast antennae were similar for cases and controls. [Although this study had strengths in its size, national coverage and sophisticated exposure assessment compared with previous studies, it was carried out during years when mobile-phone use had become fairly common, yet such usage was not accounted for.]

(c) *Cohort studies*

No data were available to the Working Group.

2.2.3 Other cancers

There have been several small ecological studies, generally of low quality, that have assessed the correlation between all cancers and distance from mobile-phone base stations (Eger *et al.*, 2004; Wolf & Wolf, 2004; Gavin & Catney, 2006; Eger & Neppe, 2009). However, the Working Group considered these studies to be uninformative for the reasons listed below.

Three ecological studies considered risk of all cancers in relation to sources of exposure to RF. Wolf & Wolf (2004) studied the incidence of all cancers around one base station located south of Netanya, Israel, which began operating in July 1996. Among the population of 622 people living within 350 m from the antenna, eight cases were identified between July 1997 and June 1998, and the rate of all cancers among these people was compared to the national rates of cancer in Israel (ratio of rates, 4.15; no confidence intervals provided). [The Working Group considered this study to be uninformative for various reasons, including its small size, unclear method of case ascertainment, crude analyses including incidence rate computed without age standardization, and other methodological limitations.]

Prompted by a reported clustering of cancer cases around a communication mast in Cranlome, Northern Ireland, an ecological study of cancer risk was carried out during 2001–02 (Gavin & Catney, 2006). The mast was erected in 1989, and was taken down in 2002. The Northern Ireland Cancer Registry was the source of case ascertainment. The rates of incidence of groups of cancer in several concentric geographical areas (up to 5 km) were compared with national rates of cancer incidence. The SIR for all cancers was 0.94 (95% CI, 0.88–0.99) for men and 1.00 (95% CI, 0.94–1.06) for women, while the SIR was 101 (95% CI, 79–104) for brain and 99 (95% CI, 74–124) for lymphoma and leukaemia. [The Working Group considered this study to be uninformative due to its small size, the fact that the number of cases was not reported and the absence of evaluation of exposure to RF radiation.]

Eger *et al.* (2004) studied the incidence of all cancers between 1994 and 2003 in areas determined by circles of radius 400 m around two mobile-phone base stations located in Naila, Germany. The first base station became operational in 1993 and the second in 1997. Streets

within and without the area were randomly selected, and the patient databases of general practitioners were searched for cases living the entire period of 10 years at the same address. [The completeness of the ascertainment appeared to be 90%.] The proportion of new cases of cancer was significantly higher among those patients who had lived for the past 10 years at a distance of up to 400 m from the cellular transmitter site, compared with patients living further away. [The Working Group considered this study uninformative due to the small and ill-defined study base and crude statistical methodology.] The same authors investigated the incidence of cancer around a mobile-phone base station in Westphalia, Germany, between 2000 and 2007 (Eger & Neppe, 2009). Twenty-three cases were identified by door-to-door interviews. The authors compared the incidence of all cancers in the 5 years immediately after installation of the mast to that in later years, and found a statistically significant increase in incidence 5 years after the base station started transmission. [The Working Group considered this study to be uninformative due to its small size and crude statistical methodology.]

Five additional studies (Dolk *et al.*, 1997a, b; Ha *et al.*, 2003; Park *et al.*, 2004; Meyer *et al.*, 2006) described information on additional cancer sites (Table 2.10, and see Section 2.2.1). [The interpretation of these results was limited by the small numbers and crude exposure classification.]

2.3 Exposure from mobile phones

With continuing changes in technology, use of mobile phones has become widespread over the last two decades. As a result, the population exposed to RF radiation has greatly increased and is still expanding, with more and more children among its number. Over these two decades, there has been rising concern regarding the potential health risks associated with use of mobile phones, particularly the possibility of increased risk of cancer of the brain. These concerns have stimulated a diverse programme of research, including epidemiological studies carried out to assess the association of mobile-phone use with risk of cancer of the brain and other diseases. The strength of epidemiological studies is obviously the capacity to directly assess the risks associated with use of mobile phones in the general population; however, the observations collected in these studies clearly only address the various exposure scenarios that existed up to the time of observation. Thus the studies carried out to date include few participants who have used mobile phones for > 10–15 years. Any risks that might be associated with lengthier exposure or with a longer interval since first exposure would not be captured by existing studies.

Three types of study design have been applied to address the question whether an increased risk of cancer is associated with RF emitted by mobile phones. These are ecological studies (in particular, observations of time trends in disease rates), case–control studies, and cohort studies. The strengths and limitations of each of these designs in general have been well described. Here, the Working Group focused on the characteristics of these designs as applied to the investigation of the potential risks of mobile-phone use.

Ecological studies provide only indirect evidence on the potential risks associated with mobile-phone use. The general approach involves comparison of time trends in mobile-phone use with time trends in disease indicators, assessing whether the trends are parallel, and allowing for a potential lag in relationships. Over the last few decades, several factors have affected trends in incidence and mortality for cancer of the brain, in particular, the increasing availability of sensitive imaging technology (computed tomography, CT, and magnetic resonance imaging, MRI) for detecting cancers of the brain, which is likely to have had a variable influence on changes in diagnostic practices, depending on country. Consequently, the interpretation of time trends is

Table 2.10 Ecological studies of other cancers and environmental exposure to radiation from transmitters of radiofrequency signals

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95%CI)	Covariates	Comments
Dolk *et al.* (1997a) United Kingdom	Around 408 000	1974–86	Distance to Sutton Coldfield radio and TV transmitter	All cancers	Distance 0–2 km Distance 0–10 km Stone's *P* value	703 17 409	1.09 (1.01–1.17) 1.03 (1.02–1.05) Unconditional $P = 0.001$ Conditional $P = 0.462$	Region	
				Skin melanoma	0–2 km	13	1.43 (0.83–2.44)		
				Eye melanoma		0	0 (0–4.22)		
				Male breast		1	1.64 (0.04–9.13)		
				Female breast		107	1.08 (0.90–1.31)		
				Lung		113	1.01 (0.84–1.21)		
				Colorectal		112	1.13 (0.94–1.35)		
				Stomach		33	0.75 (0.54–1.06)		
				Prostate		37	1.13 (0.82–1.55)		
				Bladder		43	1.52 (1.13–2.04)		
				Skin melanoma	0–10 km	189	0.96 (0.83–1.11)	Region	
				Eye melanoma		20	1.16 (0.75–1.80)		
				Male breast		15	0.99 (0.60–1.64)		
				Female breast		2412	1.05 (1.01–1.10)		
				Lung		3466	1.01 (0.98–1.05)		
				Colorectal		2529	1.03 (0.99–1.07)		
				Stomach		1326	1.06 (1.01–1.12)		
				Prostate		785	1.03 (0.96–1.11)		
				Bladder		788	1.08 (1.01–1.16)		
Dolk *et al.* (1997b) United Kingdom	Around 3 390 000	1974–86	Distance to radio and TV transmitters in United Kingdom (excluding Sutton Coldfield)	Skin melanoma	0–2 km	51	1.11 (0.84–1.46)	Region	
				Bladder		209	1.08 (0.94–1.24)		
				Skin melanoma	0–10 km	1540	0.90 (0.85–0.94)		
				Bladder		8307	1.09 (1.06–1.11)		

Table 2.10 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95%CI)	Covariates	Comments
Ha *et al.* (2003) Republic of Korea	From 3 152 to 126 523 persons per area (total not given)	1993–96	kW	Breast cancer	High-power (≥ 100 kW) *vs* low-power (50 kW) transmitter sites	39.7/33.6 per 100 000 person-years	1.2 (0.8–1.7)	Age	
			Transmitter power (kW)	Breast cancer	Sites with transmitter power:				
					100 kW	29	1.29 (0.86–1.86)		
					250 kW	20	0.88 (0.54–1.36)		
					500 kW	41	0.90 (0.64–1.23)		
					1500 kW	3	2.19 (0.45–6.39)		
Park *et al.* (2004) Republic of Korea	8 115 906	1993–95	Regions including AM-radio broadcasting towers of > 100 kW	All cancer	Total exposed *vs* control (unexposed)	6191	1.29 (1.12–1.49)	Age	Direct standardized MRRs are given.
				Oral cavity and pharynx		14	1.21 (0.41–3.57)		
				Oesophagus		49	1.20 (0.71–2.03)		
				Stomach		403	1.18 (0.96–1.44)		
				Colorectum including anus		78	1.33 (0.83–2.11)		
				Liver, including intrahepatic duct		271	1.01 (0.80–1.27)		
				Pancreas		74	1.52 (0.97–2.39)		
				Lung, including trachea		232	1.08 (0.84–1.38)		
				Thyroid		7	1.35 (0.22–8.19)		
				Breast		22	1.38 (0.63–3.02)		
				Bone and connective tissue		8	1.05 (0.21–5.22)		
				Urinary bladder		16	1.13 (0.48–2.65)		
				Skin		8	1.72 (0.36–8.21)		

Table 2.10 (continued)

Reference, study location	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95%CI)	Covariates	Comments
Meyer *et al.* (2006) Germany	177 428 persons living in 48 municipalities in Bavaria		Presence of mobile-telephone relay stations, classified into three categories of relay-station coverage	Breast Brain and CNS Thyroid		NR	NR		Incidence of all cancers combined was not found to be elevated in municipalities with mobile-telephone relay stations. Specific cancers not heterogeneously distributed

AM, amplitude modulation; CNS, central nervous system; kW, kilowatt; MRR, mortality rate ratio; NR, not reported; TV, television

complicated. Nonetheless, the ecological studies provide evidence for consideration in the assessment of the coherence of a causal association of mobile-phone use with cancer of the brain.

The critical evidence comes primarily from case–control studies, as only few cohort studies have been carried out. The basic design of most case–control studies reviewed in this section has involved interviews with cases (most studies are of cancer of the brain) and with appropriate controls; the interviews characterize use of mobile phones, exposures to other sources of RF radiation (e.g. cordless phones) in some instances, potential confounding factors, and other information. The critical methodological concerns around interpretation of the findings of case–control studies of mobile-phone use involve the comparability of cases and controls, the potential for selection bias, and information bias, particularly in ascertainment of exposure to RF radiation from mobile-phone use. Confounding is a less serious concern because, apart from age, the only well-established causal factor for cancer of the brain is ionizing radiation, and also because in the general population the distribution of exposures, primarily from diagnostic irradiation, is unlikely to introduce substantial confounding.

Information bias related to exposure assessment has been a principal concern in interpreting the findings of case–control studies. The investigators have developed interview and questionnaire approaches for ascertaining mobile-phone use and exposure characteristics that attempt to capture the full exposure profile. Key exposure metrics have included the duration of use, call frequency, and cumulative use indicators, the types of device used, and various potential modifiers of exposure, such as use of a hands-free device and the laterality of use. With this approach, some degree of non-differential (random) misclassification of exposure to RF radiation is unavoidable. In studies of the association between protracted exposures and risk of cancer, a related concern is that the key exposure metrics used may not capture the etiologically relevant period of a person's exposure profile (for example, if the effect of a hazard does not persist indefinitely, or appears only after an induction and latency period). Additionally, as in any case–control study, there is the possibility of differential recall according to case status regarding mobile-phone use and other items. Such bias may be in the direction of underreporting, if, for example, cases with tumours of the brain had diminished cognitive function. The bias may be in the direction of over-reporting if, for example, cases were more likely to recall events that might have led to their disease. A validation study carried out with the INTERPHONE Study demonstrated non-differential information bias, as well as the possibility of greater recall of temporally remote use by cases compared with controls (Vrijheid *et al.*, 2009a, b). There is the additional possibility that the degree of measurement error varies from study to study, depending on the interview approach and other factors. While random misclassification generally reduces associations, differential misclassification may increase or decrease observed associations from the "true" underlying association.

Selection bias may also affect the results. Selection bias from two sources is of potential concern: specifically, differential participation by cases and controls that is determined by factors influencing likelihood of exposure. Additional selection bias can arise from the process used to select cases and controls, such that the association is distorted from that in the underlying population. This bias is of particular concern in case–control studies involving cases selected from hospitals or other medical institutions, as the factors that lead to hospitalization and diagnosis may also be associated with the exposure(s) under investigation. Selection bias may reduce or increase the observed association.

In interpreting the results of the case–control studies, consideration was given to the net consequences of selection bias and information

bias to answer the question as to whether the observed association(s) could reflect bias (at least in part), rather than causation. The judgment of the Working Group as to the potential consequences of bias was critical to the classification of the evidence from humans. The complexities in interpretation of the findings of case–control studies of mobile phones and cancer of the brain have been reviewed recently (Ahlbom *et al.*, 2009; Saracci & Samet, 2010).

2.3.1 Cancer of the brain

(a) Ecological studies

Multiple ecological studies have been published that compare time trends in use of mobile phones and incidence and mortality rates of various cancers, primarily brain (Table 2.11). [Because these studies provided only limited and indirect evidence on the risk of cancer potentially associated with mobile-phone use, the Working Group presented a brief synthesis only.] These included two time-trend studies (Lönn *et al.*, 2004; Deltour *et al.*, 2009) in the combined Nordic countries, two in the United Kingdom (Nelson *et al.*, 2006; de Vocht *et al.*, 2011a), three in parts of the USA (Muscat *et al.*, 2006; Propp *et al.*, 2006; Inskip *et al.*, 2010), one each in Japan (Nomura *et al.*, 2011), New Zealand (Cook *et al.*, 2003), Switzerland (Röösli *et al.*, 2007) and Israel (Czerninski *et al.*, 2011), and one in a set of eleven countries (Saika & Katanoda, 2011). Most studies provided some data on the temporal pattern of increasing use of mobile phones, based mostly on annual numbers of private subscriptions and, in a few instances, on estimated prevalence of use. The information on use of mobile phones clearly demonstrated the rapid increase between 1985 and 2000; in some countries, the increase started in about 1990, while in others the increase began later in that decade. In some countries, the reported number of subscriptions had approached the total population of the country in 2000. The number of subscriptions is a surrogate for population exposure to RF radiation, but the number does not reflect temporal changes in patterns of actual usage. Most of these ecological studies had used rates of cancer incidence calculated from data obtained from national or subnational cancer registries, while two studies used mortality rates. In most of these studies, the temporal association between trends in use of mobile phones and cancer incidence was assessed informally and descriptively. [The geographical correlation study carried out in several states of the USA (Lehrer *et al.*, 2011) failed to adequately account for population size and composition.]

Studies that covered a long period between increasing use of mobile phones among the population under investigation and available data on cancer incidence from high-quality cancer registries were most informative for evaluating time trends. In Scandinavia, the rise in use of the mobile phone occurred relatively early. The reported prevalence of mobile-phone use among men aged 40–59 years was 7% in 1989 and reached 28% in 1993 (Deltour *et al.*, 2010). No change in trends in cancer incidence was observed between 1993 and 2003 for this age group, which had the highest proportion of people who started using mobile phones at an early stage (Deltour *et al.*, 2009). In the USA, the use of mobile phones started to increase somewhat later; about 100 million subscribers were registered in 2000, i.e. 36% of the population.(Inskip *et al.*, 2010). According to data collected by the Surveillance, Epidemiology, and End Results (SEER) Program, age- and sex-specific trends and overall temporal trends in rates of incidence of brain cancer in the USA were flat or downward between 1992 and 2006, with the exception of women aged 20–29 years (Inskip *et al.*, 2010). In this age group, a statistically significant increasing trend was driven by the rising incidence in tumours of the frontal lobe. [It is the temporal lobe that is most heavily exposed to radiation when using a mobile phone at the ear (Cardis *et al.*, 2008).]

Table 2.11 Time trends in use of mobile phones and cancer occurrence

Reference	Location	Exposure data	Trend in exposure	Organ site	Period of cancer occurrence	Cancer data	Cancer trend	Comments
Cook *et al.* (2003)	New Zealand	Proportion of mobile-phone subscribers in the New Zealand population	Sharp increase from 1987 (1%) to 1998 (> 30%), particularly since 1993 (5%)	All brain and salivary gland; temporal lobe; parietal lobe	1986–98	Incidence rates from New Zealand Cancer Registry	Flat trends from 1986 to 1998	No apparent impact of mobile-phone use on incidence of brain cancer. This study could only detect a risk if it occurred within 4 yr of first exposure
Hardell *et al.* (2003)	Sweden	None	Presumably sharp increases between 1980s and 2000	Vestibular schwannoma	1960–98	Incidence rates from Swedish Cancer Registry	Increase from 1960 to 1985, then rather flat	No effect of mobile-phone trends. Too early
Lönn *et al.* (2004)	Denmark, Finland, Norway, Sweden	Proportion of mobile-phone subscribers per year in each country	Sharp increase from 1987 (1–2%) to 1998 (30–50%) particularly after 1993	All brain and subtypes	1969–98	Incidence rates from Nordic National Cancer Registries	Gradual increase from 1968–1983; flat from 1983–96; slight upticks in 1997 and 1998	No apparent impact of mobile-phone use on incidence of brain cancer. Long-standing, high-quality registries. Increased incidence in late 1970s and early 1980s coincides with improvements in diagnosis. This study could only detect a mobile-phone-related risk if it occurred within about 5 yr of first exposure.
Muscat *et al.* (2006)	USA (SEER Program); 17 registries; about one quarter of the USA population	Unclear	From 0% to about 50% of the population; "exponential increase"	Neuronal tumours	1973–2002	Incidence rates from SEER	No change in incidence between two periods (1973–85 and 1986–2002)	No apparent impact of mobile-phone use on incidence of neuronal tumours. No data on year-by-year variability. Not clear when the number of users increased, probably in the early to mid-1990s. Neuronal tumours are extremely rare.

Table 2.11 (continued)

Reference	Location	Exposure data	Trend in exposure	Organ site	Period of cancer occurrence	Cancer data	Cancer trend	Comments
Nelson *et al.* (2006)	England and Wales, United Kingdom	Active mobile-phone subscriptions by year, 1987–2004	Very little before 1993; gradual increase to 1997 (10 million) then sharp annual increase to 2004 (60 million)	Acoustic neuroma	1979–2001	Incidence rates from National Cancer Registry for England and Wales	Gradual increase from 1980 to 1990; sharp increase to 1997; decline to 2000. Rise and decline of acoustic neuroma attributed to changes in diagnosis and registration	No apparent impact of mobile-phone use on incidence of acoustic neuroma. The reason for decline in rates after 1997 is uncertain, but its magnitude illustrates the difficulty of detecting a signal if there is one, against the background noise of statistical variability and methodological challenges. The number of subscriptions, approx. 60 million, is clearly in excess of the number of people with subscriptions in England and Wales.

Table 2.11 (continued)

Reference	Location	Exposure data	Trend in exposure	Organ site	Period of cancer occurrence	Cancer data	Cancer trend	Comments
Propp *et al.* (2006)	Several centres in the USA	None	NR	Acoustic neuroma (vestibular schwannoma)	Los Angeles 1975–98; other centres 1985–99	Incidence rates from the Central Brain Tumor Registry of the USA, and the Los Angeles County Cancer Surveillance Program	Modest, but discernable gradual increases over the period of observation	No apparent impact of mobile-phone use on incidence of acoustic neuroma. Modest increase in risk over the period of time studied (1970s to 1990s) could be due to improvement in diagnosis and registration or to some environmental factor. While the authors present no data on trends in mobile-phone use, it is likely that use increased in the early to mid-1990s. This study could only detect a mobile-phone-related risk if it occurred within about 5 yr of first exposure.
Röösli *et al.* (2007)	Switzerland	Prevalence of mobile phone use by year, with mortality rates	None before 1987; slow increase to 1996 (< 10%) and then sharp increase to 2000 (> 60%)	All brain (ICD-8 code 191)	1969–2002	Mortality rates from Swiss Federal Statistical Office	Gradual increase from 1969 to 2002, reaching a plateau after 1997. Smaller increase in rates after 1987 than before. For the whole period, there was a significant increase for men and women in older age groups, but not in younger ones. From 1987 onwards, rather stable rates in all age groups.	No apparent impact of mobile-phone use on incidence of cancer of the brain. High-quality mortality data. Authors quantify difficulty in detecting risk in such an ecological study. Improvements in survival may influence trends in mortality.

Table 2.11 (continued)

Reference	Location	Exposure data	Trend in exposure	Organ site	Period of cancer occurrence	Cancer data	Cancer trend	Comments
Deltour *et al.* (2009)	Denmark, Finland, Norway, Sweden	Unclear	Use increased from zero in the mid-1980s to 'widespread' in the early 1990s to 'sharply increased' in the mid-1990s.	Glioma and meningioma	1974–2003	Incidence rates from Nordic National Cancer Registries	Very slight increases in incidence from 1974 to 1997; no change after 1998	No apparent impact of mobile-phone use on incidence of cancer of the brain. High-quality registration. Up to 10 yr potential latency
Hardell & Carlberg (2009)	Sweden	None	Presumably sharp increases between 1980s and 2000	Brain, age > 19 yr Acoustic neuroma, age > 19 yr	1970–2007	Incidence rates from Swedish Cancer Registry	Changing annual incidence: 1970–79 (+0.15%) 1980–89 (+1.54%) 1990–99 (–0.25%) 2000–07 (+1.26%) 1970–79 (–1.66%) 1980–89 (+4.86%) 1990–99 (+0.66%) 2000–07 (–7.08%)	No evidence of an impact of mobile-phone use on the risk of acoustic neuroma. No or very weak evidence of an effect of phone use on risk of tumours of the brain. Slightly stronger evidence for increased risk of astrocytoma in the most recent period
Inskip *et al.* (2010)	USA (SEER Program); nine state or regional population-based cancer registries	Number of mobile-phone subscribers in USA by year	From very few in 1990 to 25 million in 1995; 100 million in 2000 and 200 million in 2005	All brain, excluding meningioma and lymphoma	1977–2006	Incidence rates from SEER	Gradual increase in risks from 1977 to 1985; since 1986 the pattern is flat or slightly decreasing. Some age/sex subgroups show increasing trends in some subtypes	No apparent impact of mobile-phone use on incidence of cancer of the brain. Very large numbers of cases. Up to 10 yr of potential latency

Table 2.11 (continued)

Reference	Location	Exposure data	Trend in exposure	Organ site	Period of cancer occurrence	Cancer data	Cancer trend	Comments
Czerninski *et al.* (2011)	Israel	None	Exposure trend not shown but presumably sharp increase between mid-1980s and 2006	Parotid gland	1970–2006	Incident numbers of cases from Israel National Cancer Registry	Approximate tripling of number of tumours of the parotid gland, with increase starting around 1977 and picking-up around 1990	Authors state that population growth explains part of the increase, but they do not acknowledge the role of ageing of the population. Rates would be more convincing than numbers. While numbers increased greatly after 1998, there were, nevertheless, important increases in numbers of cases before mobile phones could plausibly have caused large numbers of cases.
de Vocht *et al.* (2011a)	England	Mobile-phone subscriptions	Sharp increase from 0 in 1985 to 10 million in 1997 to > 50 million in 2003	All brain and each of 11 subsites	1998–2007	Incidence rates from United Kingdom Office of National Statistics	Linear regression for each of 24 sex/site categories. No significant trend for all cancers combined. Significant increase in incidence of tumours of temporal lobe and decreases in tumours of parietal lobe	No apparent impact of mobile-phone use on incidence of cancer of the brain, except for a small but unconvincing increase in incidence of tumours of the temporal lobe. Up to 10 yr of potential latency. The number of subscriptions, approx. 50 million in 2003, is clearly in excess of the number of people with subscriptions in England.

Table 2.11 (continued)

Reference	Location	Exposure data	Trend in exposure	Organ site	Period of cancer occurrence	Cancer data	Cancer trend	Comments
Nomura *et al.* (2011)	Osaka	None	Presumably sharp increases between 1980s and 2000	Intracranial	1975–2004	Incidence rates from Osaka Cancer Registry	Age 0–1 yr, flat; age 20–74 yr, flat until 1999 then slight decline; age 75 yr, sharp increase to 1983 then flat	No increase in incidence rates in recent years. Increasing rates in early years may have been due to diagnostic improvements.
Saika & Katanoda, (2011)	Study involved 11 countries: Japan, Hong Kong Special Administrative Region, Republic of Korea, USA, Australia, the Russian Federation, United Kingdom, Italy, Spain, France, Germany	None	Presumably sharp increases between 1980s and 2000	Brain and CNS	1990–2005	Mortality rates from WHO database	In most of the 22 country/sex data sets, there was a rather flat or declining rate; only in the Russian Federation and Spain was there an increase among females	No apparent increase in mortality from cancer of the brain. Mortality rates may reflect trends in diagnostic standards and in survival.

NR, not reported; SEER, Surveillance, Epidemiology and End Results; yr, year

In another study, trends in rates of newly diagnosed cases of cancer of the brain in England between 1998 and 2007 were examined (de Vocht *et al.*, 2011a). Overall rates of incidence of cancer of the brain in males or females, or in any specific age group were not increased. However, the incidence of tumours of the temporal lobe increased between 1998 and 2007. In a subsequent letter, the same authors reported separate time trends for the periods 1979–99 and 2000–08. For men, a linear regression of age-adjusted rates showed an overall annual increase in 2000–08 of 3.3% (95% CI, 1.1–5.4), whereas it was 2.0% (95% CI, 1.4–2.6) for 1979–99 (de Vocht *et al.*, 2011b). [The linear regression used for this analysis was not an appropriate method and therefore the 95% confidence intervals reported may not be reliable.] For women, corresponding annual increases were 2.8% (95% CI, 0.9–4.9) for 2000–08 and 1.4% (95% CI, 0.7–2.2) for 1979–99.

[The Working Group noted that time-trend analyses did not provide any indication that the rapid increase in use of mobile phones had been followed by a parallel increase in incidence rates of cancer of the brain. Increases in rates of brain tumours in the 1970s and 1980s had paralleled the introduction and distribution of new diagnostic tools, namely CT and MRI. The Working Group further noted that these descriptive analyses would be null if an excess in cancer risk from mobile-phone use became manifest only decades after phone use began, or if an increase affected only a small proportion of the cases by location.]

(b) Cohort studies

An early attempt to conduct a cohort study in the USA on cancer and mobile-phone use was halted by legal action; consequently, the study did not provide useful results (Dreyer *et al.*, 1999). A retrospective cohort study was conducted in Denmark based on the subscriber lists from the two Danish mobile-phone operating companies, including 420 095 individual (i.e. virtually all non-institutional) subscribers from 1982 to 1995. Using unique identifiers, these subscribers were linked to the Danish Cancer Registry from 1982 onwards. The linkage allowed the identification of all cancers occurring in this cohort, and notably cancers of putative target organs. Expected numbers of cases were based on rates in the Danish population. Two papers appeared, one covering cancer outcomes from 1982 to 1996 (Johansen *et al.*, 2001) and the second covering outcomes from 1982 to 2002 (Schüz *et al.*, 2006c). In the latter, more recent, analysis, the expected rates were computed with cohort members excluded from the reference population by subtracting the number of cases of cancer and person-years observed in the cohort from the corresponding figures for the total Danish population. Approximately 85% of the cohort members were males.

There were various sources of misclassification, as acknowledged by the authors. Members of the reference population, apart from cohort members, may well have used mobile phones, either with subscriptions that were not in their names (e.g. corporate accounts), or with subscriptions taken out after 1995. Moreover, a member of the cohort may have been the official subscriber to an account, but not the true user. Using information from a separate case–control study, it was estimated that as many as 39% of cohort members may not have been mobile-phone users before 1996 and as many as 16% of the reference population may have been users. Using information from Statistics Denmark, it appeared that the cohort members represented a somewhat more affluent section of the Danish population. While the investigators had no data on individual patterns of use, they had information on the year of the individual's first subscription, and this was used to compute SIRs by time since first use. The median duration of subscription among subscribers was 8 years and the maximum was 21 years.

For the entire cohort there was a slight deficit of total cancers among males (SIR, 0.93; 95% CI,

0.92–0.95), and a slight excess among females (SIR, 1.03; 95% CI, 0.99–1.07). For the main cancer types of interest, the results were similarly close to the null value, with relatively narrow confidence intervals, as shown in Table 2.12. For subtypes of cancer of the brain, most SIRs were close to the null value.

The SIR for glioma was 1.01 (95% CI, 0.89–1.14; 257 cases). The odds ratios for glioma in the two lobes closest to the ear showed conflicting results, with a SIR of 1.21 (95% CI, 0.91–1.58) for the temporal lobe and a SIR of 0.58 (95% CI, 0.36–0.89) for the parietal lobe. The SIR was lower for all other areas of the brain, although confidence intervals were overlapping. [Cardis *et al.* (2008) have reported that it is the temporal lobe of the brain that receives the highest percentage of RF radiation deposition (50%).]

The SIR for meningioma was 0.86 (95% CI, 0.67–1.09) and for acoustic neuroma (nerve sheath tumour) it was 0.73 (95% CI, 0.50–1.03). There was no trend in SIR according to years since first subscription, and the subgroup with > 10 years since first subscription had a low SIR for all tumours of the brain and nervous system (SIR, 0.66; 95% CI, 0.44–0.95). [There were few subscribers who began using a mobile phone ≥ 10 years before the end of follow-up. and there was no information on individual levels of mobile-phone use.]

The Danish subscriber cohort study was updated for occurrence of acoustic neuroma (vestibular schwannoma) until 2006 (Schüz *et al.*, 2011). This update and analysis was restricted to a large subset of subscribers and of the Danish population (2.9 million subscribers and non-subscribers) for which independent information was available on each subject's highest level of education, annual disposable income and marital status. Further to the follow-up with data from the Danish cancer registry, a clinical registry of acoustic neuroma was used to achieve completeness of case ascertainment and obtain additional tumour characteristics, such as laterality, and spread and size of the acoustic neuroma. In this cohort analysis, having a long-term mobile-phone subscription of ≥ 11 years was not related to an increased risk of vestibular schwannoma in men (RR, 0.87; 95% CI, 0.52–1.46; adjusted for sociodemographic factors); and no cases of acoustic neuroma occurred among long-term female subscribers versus 1.6 cases expected. Although 53% of Danes reported that they mainly used their phones on the right side, with 35% preferring the left side and 13% having no preferred side, based on data from the launch of a prospective cohort study described in Schüz *et al.*, 2011), acoustic neuroma in the subscriber cohort occurred equally on both sides (48% of tumours were on the right side, with no change in this proportion over time). Acoustic neuromas in long-term male subscribers were not larger than those in non-subscribers and short-term subscribers (mean diameter, 14.6 versus 15.9 mm).

(c) Case–control studies

There have been many case–control studies of tumours of the brain in relation to use of mobile phones: a series from one group in Sweden (this study also included cordless phones), an IARC-coordinated series from 13 countries known as INTERPHONE (this study included use of cordless phones among the unexposed group), and several others, including three from the USA, and one each from Finland, France, Greece and Japan. Some studies considered all major types of tumours of the brain, while others considered glioma and meningioma, or glioma only, or acoustic neuroma only. The studies are presented below by major tumour type. Most studies were based on interviews with study subjects or proxies, and involved questions on history of mobile-phone use. Various exposure metrics were used in the different studies, including binary indicators of ever versus never use, metrics of duration of use, frequency of use, and time since start of use. In addition, some analyses

Table 2.12 Cohort study of cancer of the brain and use of mobile phones

Reference, study location and period	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Comments
Schüz *et al.* (2006c) Denmark,1982–2002	420 095, 357 553 men, 62 542 women	1982–2002	Subscribers to mobile-phone service	All cancers	Ever subscribed	14 291	0.95 (0.93–0.97)	Update of Johansen *et al.* (2001). Median time since first subscription, 8 yr. Expected numbers derived from Danish National Cancer Registry after excluding cohort members from the population. Questionable correspondence between mobile-phone subscriptions and use levels.
					Ever subscribed: men	11 802	0.93 (0.92–0.95)	
					Ever subscribed: women	2 447	1.03 (0.99–1.07)	
				Brain, CNS	Ever subscribed	580	0.97 (NR)	
				Brain, CNS	Ever subscribed: men	491	0.96 (0.87–1.05)	
				Brain, CNS	Ever subscribed: women	89	1.03 (0.82–1.26)	
				Brain, CNS	Latency, < 1 yr since start	51	0.90 (0.67–1.18)	
				Brain, CNS	Latency, 1–4 yr since start	266	1.03 (0.91–1.17)	
				Brain, CNS	Latency, 5–9 yr since start	235	0.96 (0.84–1.09)	
				Brain, CNS	Latency, ≥ 10 yr since start	28	0.66 (0.44–0.95)	
				Glioma (191–191.9)	Ever subscribed	257	1.01 (0.89–1.14)	
				Temporal lobe (191.2)	Ever subscribed	54	1.21 (0.91–1.58)	
				Parietal lobe (191.3)	Ever subscribed	21	0.58 (0.36–0.89)	
				Meningioma (192.1)	Ever subscribed	68	0.86 (0.67–1.09)	
				Nerve sheath tumours (192.0) [a]	Ever subscribed	32	0.73 (0.50–1.03)	

[a] Includes other rare tumours of the nerve sheath

CI, confidence interval; CNS, central nervous system; NR, not reported; yr, year or years

considered modifiers of exposure, such as laterality of mobile-phone use. The latter was based on the premise that if there were a risk related to mobile-phone use, it should manifest itself in a greater proportion of tumours on the side of the head corresponding to the subject's preferred side of phone use. Some studies analysed exposure in relation to the lobe in which the tumour appeared, based on the premise that some lobes absorb more RF radiation than others.

(i) Glioma

See Table 2.13

A case–control study of cancer of the brain was conducted in five academic medical centres in the north-eastern USA during 1994–1998 (Muscat *et al.*, 2000). Interviews were conducted with the cases (n = 469), mainly patients with glioma, and with controls (n = 422) selected from the same medical centres. Analysis of reported histories of mobile-phone use, adjusting for sociodemographic factors, study centre, proxy status, and date of interview, yielded a set of odds-ratio estimates that showed no effect, whether by various exposure metrics, anatomical location of the tumour, or histological subtypes. The only exception was an odds ratio of 2.1 (95% CI, 0.9–4.7) for neuroepitheliomatous tumours (14 exposed cases). [The Working Group noted that the highest prevalence of these tumours occurred in the temporal lobe.] The longest duration of use considered was ≥ 4 years. [The numbers of cases were small, exposure levels were low: of the 422 controls, 346 had never used a mobile phone and 22 had used a mobile phone for ≥ 4 years.]

Inskip *et al.* (2001) conducted a case–control study of tumours of the brain in three centres between 1994 and 1998. A total of 489 cases of glioma were interviewed, as were 799 controls. Compared with non-users, self-reported regular use of mobile phones was not associated with excess risk of glioma (OR, 0.8; 95% CI, 0.6–1.2). Based on very small numbers, there was no indication of excess risk among people with the heaviest (cumulative use, > 500 hours) or longest (5 years or more) use of mobile phones, or any relationship between reported laterality of use and laterality of the tumours, or any relationship with neuroepitheliomatous tumours (OR, 0.5; 95% CI, 0.1–2.0; eight exposed cases). [Of the 799 controls, 625 had never or rarely used a hand-held mobile phone and only 50 had used a hand-held mobile phone before 1993.]

In a case–control study in Finland, the researchers enrolled cases of tumours of the brain and salivary gland occurring in 1996, as well as a 5 : 1 control series selected from the general population (Auvinen *et al.*, 2002). There were 198 cases of glioma. Each subject was linked to a list of all subscribers to the two mobile-phone companies operating in Finland, to establish whether the subject had been a subscriber, for how long, and what type of phone he or she was using (analogue/digital). Linkage of records to the census allowed the investigators to ensure that the case and control series were similar in occupational, socioeconomic and urban/rural characteristics. The odds ratio for glioma was 1.5 (95% CI, 1.0–2.4) for those who had ever had a mobile-phone subscription (about 12% of all subjects), and 1.7 (95% CI, 0.9–3.5) for those who had had a subscription for > 2 years (< 4% of all subjects). When examined separately, the ever-users of analogue phones had an odds ratio for glioma of 2.1 (95% CI, 1.3–3.4) and ever-users of digital phones had an odds ratio of 1.0 (95% CI, 0.5–2.0). [A strength of this study was the linkage of cancer records, population-register records, and mobile-phone subscription records. It was limited by small numbers, inability to assess impact of use of mobile phones for > 2 years, and uncertainty about the correspondence between subscription to a mobile-phone service and individual use of mobile phones.]

Two hospital-based case–control studies (Gousias *et al.*, 2009; Spinelli *et al.*, 2010), one in Greece and the other in France, examined associations between glioma and malignant tumours

of the brain, respectively, and mobile-phone use. The results are summarized in Table 2.13. Neither study was informative due to small numbers and unclear methods of exposure assessment.

The INTERPHONE study, a multicentre case–control study on use of mobile phones and various types of tumour of the brain, is the largest study on this topic so far. The study was coordinated by IARC and conducted in 16 study centres in 13 countries with a common core protocol (Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, and the United Kingdom). A detailed description of the study design, epidemiological methods and study population can be found in Cardis *et al.* (2007). In brief, the source population was generally restricted to major metropolitan areas where mobile phones were first introduced and where most of the population was considered to be unlikely to leave the region for diagnosis and treatment. Residents aged between 30 and 59 years were eligible for the study, but somewhat larger age ranges were applied in some of the centres. The study periods also varied somewhat across centres, ranging from 2 to 4 years between 2000 and 2004. Eligible cases were ascertained rapidly through neurological and neurosurgical facilities in the study regions, and completeness of ascertainment was checked with secondary sources (Cardis *et al.*, 2007). Cases had a histologically confirmed or unequivocal imaging-based diagnosis of a first primary glioma, meningioma or acoustic neurinoma. Three centres also included malignant tumours of the parotid gland, and Japan additionally included pituitary tumours. Population controls were randomly selected from population registries (part of Canada, Denmark, Finland, Germany, Italy, Norway, Sweden), electoral lists (Australia, part of Canada, France, New Zealand), patient lists from general practice (United Kingdom) or by random-digit dialling (part of Canada, France, Japan). Controls were individually (part of Canada, France, Japan, New Zealand, United Kingdom) or frequency-matched (remaining countries) to cases on year of birth (within categories of 5 years), sex and study region. One control was recruited for each patient with a tumour of the brain, two for each patient with acoustic neuroma, and three for each patient with a tumour of the parotid gland.

All consenting subjects were interviewed face-to-face by trained interviewers by use of a computer-assisted personal interview (CAPI) whenever possible. If participants had died or were too ill to be interviewed, a proxy was interviewed. The questionnaire covered demographic factors, potential confounders and risk factors for the diseases of interest, including detailed questions on use of mobile phones and other wireless-communication devices. A regular mobile-phone user was defined as having used a mobile phone for at least one call per week during 6 months or more.

Since the first publications of national results in 2004 (Christensen *et al.*, 2004; Lönn *et al.*, 2004), numerous papers have presented results from single countries (Christensen *et al.*, 2005; Lönn *et al.*, 2005; Schoemaker *et al.*, 2005; Hepworth *et al.*, 2006; Schüz *et al.*, 2006a, b; Takebayashi *et al.*, 2006, 2008; Hours *et al.*, 2007; Klaeboe *et al.*, 2007; Schlehofer *et al.*, 2007; Sadetzki *et al.*, 2008; Hartikka *et al.*, 2009) or pooled results from a subset of the INTERPHONE countries, such as the five north European countries: Denmark, Finland, Norway, Sweden, and the United Kingdom (Schoemaker *et al.*, 2005; Lahkola *et al.*, 2007, 2008). In addition, various papers have addressed methodological issues such as exposure misclassification and selection bias (Samkange-Zeeb *et al.*, 2004; Berg *et al.*, 2005; Lahkola *et al.*, 2005; Vrijheid *et al.*, 2006a, b, 2009a, b). The results presented here focus on the pooled results from all countries.

The INTERPHONE Study Group (2010) published the pooled analysis of the INTERPHONE study on the risk of glioma and meningioma in relation to use of mobile phones,

Table 2.13 Case–control studies of glioma and use of mobile phones

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (1999) Sweden, 1994–96	136	Two controls per case	Population	Self-administered standardized questionnaire	48 glioblastoma, 46 astrocytoma, 19 oliodendroglioma, 3 ependymoma, 16 mixed glioma, and 4 other malignant tumours	Never use of mobile phone Ever use	 53	1.0 1.0 (0.6–1.5)	Age, sex, SEI, and year of diagnosis	
Muscat *et al.* (2000) USA, 1994–98	469	422	In-patients from five USA academic medical centres. Controls from the same hospitals as cases, from daily admission rosters	In-person interviews, history of mobile-phone use	Brain cancer (191.0–191.9)	Ever use Cumulative use (h): 0 > 0 to ≤ 8.7 > 8.7 to ≤ 60 > 60 to ≤ 480 > 480	NR 17 12 19 14	0.7 (0.5–1.1) 1.0 (0.5–2.0) 0.6 (0.3–1.3) 0.9 (0.5–1.8) 0.7 (0.3–1.4)	Age, education, sex, race, study centre, proxy, year of interview	Analyses showed no associations by year of use. Few subjects with long-term heavy exposure. Response rates were 82% for cases and 90% for controls.
	108	422			Temporal lobe	Ever use	108	0.9 (0.5–1.7)		
	60	422			Parietal lobe	Ever use	60	0.8 (0.3–2.0)		
	354	422			Astrocytic	Ever use	41	0.8 (0.5–1.2)		
	35	422			Neuro-epitheliomatous	Ever use	14	2.1 (0.9–4.7)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Inskip *et al.* (2001) USA, 1994–98	489	799	Patients admitted to the same hospitals for a variety of non-malignant conditions.	Computer-assisted, personal interview in the hospital	Glioma	Cumulative use (h):			Hospital, age, sex, race or ethnic group, proximity of residence to the hospital	There are results for other exposure metrics: average daily use, duration of use, year in which use began. Also results for acoustic neuroma, and for laterality by tumour type.
						Never or rarely used	398	1.0		
						< 13	26	0.8 (0.4–1.4)		
						13–100	26	0.7 (0.4–1.3)		
						> 100	32	0.9 (0.5–1.6)		
						> 500	11	0.5 (0.2–1.3)		
						Regular use	85	0.8 (0.6–1.2)		
						Start of use before 1993	23	0.6 (0.3–1.4)		
Auvinen *et al.* (2002) Finland, 1996	398 (198 glioma)	1990	Population Registry Centre of Finland	Information on subscriptions obtained from the two mobile-network providers operating in Finland in 1996	Glioma (191)	*Analogue*:			Age, sex	Cases, age 20–69 yr
						Ever	26	2.1 (1.3–3.4)		
						< 1 yr	4	1.6 (0.5–5.1)		
						1–2 yr	11	2.4 (1.2–5.1)		
						> 2 yr	11	2.0 (1.0–4.1)		
						Digital:				
						Ever	10	1.0 (0.5–2.0)		
						< 1 yr	3	0.8 (0.2–2.6)		
						1–2 yr	7	1.4 (0.6–3.4)		
						> 2 yr	0	0		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2002b) Sweden, 1997–2000	588	581	Population	Self-administered standardized questionnaire	415 astrocytomas, 6 medullo-blastomas, 54 oligodendro-gliomas, 11 ependymomas, 65 other/mixed gliomas, and 37 other malignant tumours of the brain	Never use of mobile/ cordless phone		1.0 (reference)	Age, sex, SEI, and year of diagnosis	Ipsilateral use of analogue phone was associated with risk of malignant tumour of the brain (OR, 1.8; 95% CI, 1.2–3.0). Ipsilateral use of digital phone was also associated with risk of malignant tumour of the brain (OR, 1.6; 95% CI, 1.1–2.4).
						Analogue, ever use	79	1.1 (0.8–1.6)		
						Digital, ever use	112	1.1 (0.8–1.5)		
						Digital, > 1–6 yr latency	100	1.1 (0.8–1.4)		
						Digital, > 6 yr latency	12	1.7 (0.7–4.3)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2006a,c) Sweden, 2000–03	317	1990	Population	Self-administered standardized questionnaire	248 astrocytomas, and 69 other malignant tumours of the brain	Never use of mobile/ cordless phone	63	1.0	Age, sex, SEI, and year of diagnosis	
						Ever use, analogue	68	2.6 (1.5–4.3)		Analogue phone: Ipsilateral use: 3.1 (95% CI, 1.6–6.2); contralateral use: 2.6 (95% CI, 1.3–5.4)
						Ever use, digital	198	1.9 (1.3–2.7)		Digital phone: Ipsilateral use: 2.6 (95% CI, 1.6–4.1); contralateral use: 1.3 (95% CI, 0.8–2.2)
						Time since start of use, analogue (yr)				
						> 1–5	0	–		
						> 5–10	20	1.8 (0.9–3.5)		
						> 10	48	3.5 (2.0–6.4)		
						Time since start of use, digital (yr)				
						> 1–5	100	1.6 (1.1–2.4)		
						> 5–10	79	2.2 (1.4–3.4)		
						> 10	19	3.6 (1.7–7.5)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2006b) Sweden, 1997–2003	905	2162	Population	Self-administered standardized questionnaire	539 high-grade astrocytomas, 124 low-grade astrocytomas, 93 oligodendrogliomas, 78 other/mixed gliomas and 71 other malignant tumours of the brain	Never use of mobile/cordless phone		1.0 (reference)	Sex, age, SEI, and year of diagnosis	Pooled analysis of case–control data for living cases ascertained from 1997–2000 and 2000–03. See also further results of analyses of these data in Hardell *et al.* (2009)
						Ever use, analogue	178	1.5 (1.1–1.9)		
						Ever use, digital	402	1.3 (1.1–1.6)		
						Time since start of use, analogue (yr)				
						> 1–5	39	1.2 (0.8–1.8)		
						> 5–10	57	1.1 (0.8–1.6)		
						> 10	82	2.4 (1.6–3.4)		
						Time since start of use, digital (yr)				
						> 1–5	265	1.2 (1.0–1.5)		
						> 5–10	118	1.7 (1.2–2.2)		
						> 10	19	2.8 (1.4–5.7)		
						Cumulative call time, analogue (h)				
						1–1000	147	1.3 (1.0–1.7)		
						1000–2000	10	3.0 (1.1–7.7)		
						> 2000	21	5.9 (2.5–14)		
						Cumulative call time, digital (h)				
						1–1000	355	1.3 (1.0–1.6)		
						1001–2000	26	1.8 (1.0–3.1)		
						> 2000	21	3.7 (1.7–7.7)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2006b) (cont.)						*Ipsilateral use, analogue:*				
					All malignant		95	2.1 (1.5–2.9)		
					High-grade astrocytoma		62	2.4 (1.6–3.6)		
					Low-grade astrocytoma		10	1.8 (0.8–4.1)		
						Contralateral use, analogue:				
					All malignant		54	1.1 (0.8–1.6)		
					High-grade astrocytoma		37	1.6 (1.0–2.5)		
					Low-grade astrocytoma		4	0.5 (0.2–1.6)		
						Ipsilateral use, digital:				
					All malignant		195	1.8 (1.4–2.4)		
					High-grade astrocytoma		127	2.3 (1.7–3.1)		
					Low-grade astrocytoma		27	1.9 (1.0–3.5)		
						Contralateral use, digital:				
					All malignant		119	1.0 (0.7–1.3)		
					High-grade astrocytoma		69	1.1 (0.8–1.5)		
					Low-grade astrocytoma		16	1.1 (0.5–2.1)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Gousias *et al.* (2009) Greece, 2005–07	41	82	Neuro-surgery patients	In-person interviews, history of mobile phone use	Glioma	Minutes per year of mobile-phone use	NR	1.00 (0.99–1.01)	Age, sex, residence area, smoking, alcohol, head trauma	Not informative because of low power and too finely resolved exposure metric
Hardell *et al.* (2010) Sweden, 1997–2003	346	343 cancer controls, 276 other controls	Swedish Death Registry	Interviews with relative of decedent	314 gliomas and 32 other malignant tumours of the brain	Never use of mobile/ cordless phone		1.0	Sex, age, SEI, and year of diagnosis	Analysis of deceased cases (and controls) only
						Ever use, analogue	61	1.7 (1.1–2.7)		
						Ever use, digital	83	1.4 (1.0–2.1)		
						Cumulative call time, analogue (h)				
						1–1000	41	1.5 (1.0–2.5)		
						1001–2000	5	1.1 (0.3–3.3)		
						> 2000	15	5.1 (1.8–14)		
						Cumulative call time, digital (h)				
						1–1000	58	1.2 (0.8–1.8)		
						1001–2000	8	2.6 (0.9–8.0)		
						> 2000	17	3.4 (1.5–8.1)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Spinelli *et al.* (2010) France, 2005	122	122	In-patients from neurosurgery departments of the same hospitals; unrelated to cancer	In-person interviews	Malignant primary tumours of the brain, 72 glioblastomas	Subscription hours/year			Sex, age	Unclear criteria for recruitment; small numbers
						0	37	1.0		
						< 4	8	0.9 (0.3–2.4)		
						4–36	58	1.4 (0.8–2.8)		
						≥ 36	13	1.1 (0.4–2.8)		
INTERPHONE Study Group (2010) Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, United Kingdom, 2000–04	2708	2972	Population (except United Kingdom: GP patients)	Interviewer-administered standardized questionnaire	Glioma (D33.0, D43.0–43.9, C71.0–71.9)	Never regular use of mobile phone	1042	1.0 (ref.)	Sex, age, study centre, ethnicity (in Israel) and education	OR highest in short-term users (start of mobile phone use, 1–4 yr before reference date) (OR, 3.77; 95% CI, 1.25–11.4, based on eight cases)
						Regular use	1666	0.81 (0.70–0.94)		
						Time since start of use (yr)				
						1.5	156	0.62 (0.46–0.81)		
						2–4	644	0.84 (0.70–1.00)		
						5–9	614	0.81 (0.60–0.97)		
						≥ 10	252	0.98 (0.76–1.26)		
						Cumulative call time with no hands-free devices (h)				
						< 5	141	0.70 (0.52–0.94)		
						5–12.9	145	0.71 (0.53–0.94)		
						13–30.9	189	1.05 (0.79–1.38)		
						31–60.9	144	0.74 (0.55–0.98)		
						61–114.9	171	0.81 (0.61–1.08)		
						115–199.9	160	0.73 (0.54–0.98)		
						200–359.9	158	0.76 (0.57–1.01)		
						360–734.9	189	0.82 (0.62–1.08)		
						735–1639.9	159	0.71 (0.53–0.96)		
						≥ 1 640	210	1.40 (1.03–1.89)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2011a) Sweden, 1997–2003	1148	2438	Population	Self-administered standardized questionnaire	Glioma	Never use of mobile/cordless phone		1.0	Sex, age, SEI, and year of diagnosis	Pooled analysis of case–control data for living cases ascertained from 1997–2000, and 2000–03, as well as case–control data for deceased cases 1997–2003.
						Ever use (mobile phone)	529	1.3 (1.1–1.6)		
						Time since start of use (yr)				
						> 1–5	250	1.1 (0.9–1.4)		
						> 5–10	156	1.3 (1.0–1.6)		
						> 10	123	2.5 (1.8–3.3)		
						Cumulative call time, mobile phone (h)				
						1–1000	427	1.2 (1.03–1.5)		
						1001–2000	44	1.8 (1.2–2.8)		
						> 2000	58	3.2 (2.0–5.1)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Cardis *et al.* (2011) Australia, Canada, France, Israel, Italy, New Zealand, 2000–04	553	1762	Population	Interviewer-administered standardized questionnaire	Glioma (D33.0, D43.0–43.9, C71.0–71.9)	*RF TCSE (J/kg)*			Sex, age, study centre, ethnicity (in Israel) and education	Interpretation of OR is most meaningful when compared with the corresponding OR for comparable exposure surrogates of mobile-phone use. When stratified for different time windows of time before diagnosis, the OR tended to increase with increasing TSCE for use ≥ 7 yr in the past. For the highest exposure quintile: OR, 1.91 (95% CI, 1.05–3.47)
						< 76.7	67	0.76 (0.53–1.09)		
						76.7–	68	0.94 (0.66–1.35)		
						284.1–	60	0.80 (0.54–1.18)		
						978.9–	57	0.89 (0.61–1.30)		
						3123.9+	103	1.35 (0.96–1.90)		
						Case-only analyses:				
						Ever regular user	30	1.35 (0.64–2.87)		
						Time since start of use (yr)				
						1–4	12	1.37 (0.59–3.19)		
						5–9	7	0.72 (0.27–1.90)		
						≥ 10	11	2.80 (1.13–6.94)		
						Cumulative call time without hands-free devices (h)				
						< 39	6	1.19 (0.40–3.51)		
						39–220	4	0.93 (0.27–3.14)		
						220–520	5	1.38 (0.42–4.53)		
						520–1147	10	2.55 (0.94–6.91)		
						> 1147	5	0.99 (0.30–3.27)		

Table 2.13 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Larjavaara *et al.* (2011) Denmark, Finland, Germany, Italy, Norway, Sweden, south-eastern England, 2000–04	888		Population (except United Kingdom: GP patients)	Interviewer-administered standardized questionnaire	Glioma (D33.0, D43.0–43.9, C71.0–71.9)	Never-regular use of mobile phone	91		Country, sex, age group, and SES	Case–case analysis
						Regular use	107	0.80 (0.56–1.15)		ORs are for a distance of ≤ 5 cm between the glioma midpoint and the typical source of mobile-phone exposure in regular mobile-phone users, compared with never-regular users
						Duration of use (yr)				
						1.5–4	65	0.85 (0.57–1.25)		
						5–9	30	0.71 (0.43–1.18)		
						≥ 10	10	0.85 (0.39–1.86)		
						Cumulative call time (h)				
						0.001–46	33	0.82 (0.51–1.31)		
						47–339	38	0.97 (0.60–1.56)		
						> 339	30	0.58 (0.35–0.96)		
						Laterality of use				
						Ipsilateral	51	0.80 (0.52–1.22)		
						Contralateral	37	0.77 (0.47–1.24)		
						Never regular use of mobile phone	91	1.30 (0.95–1.80)	Within-subject comparison	Case–specular analysis
						Regular use	107	1.19 (0.89–1.59)		
						Duration of use (yr)				
						1.5–4	65	1.15 (0.80–1.66)		
						5–9	30	1.04 (0.61–1.76)		
						≥ 10	10	2.00 (0.68–5.85)		
						Cumulative call time (h)				
						0.001–46	33	1.39 (0.81–2.38)		
						47–339	38	1.21 (0.74–1.97)		
						> 339	30	1.00 (0.59–1.69)		

GP, general practitioner; h, hour; NR, not reported; OR, odds ratio; RF, radiofrequency radiation; SEI, socioeconomic index; SES, socioeconomic status; TCSE, total cumulative specific energy; yr, year

and included 2708 cases of glioma and 2972 controls. The study included 252 cases of glioma and 232 controls who had first used a mobile phone at least 10 years before the reference date. Participation rates were 64% among cases of glioma and 53% among controls. There was wide variation in participation rates for controls between study centres (42–74%).

For regular users, the odds ratio for glioma was 0.81 (95% CI, 0.70–0.94) (Table 2.13). In most study centres, odds ratios of < 1.0 were also seen for all categories of time since start of use and of cumulative number of calls. [The reason for these low odds ratios was not established. While it is plausible that this may in part reflect selection/participation biases, sensitivity analyses carried out by Vrijheid *et al.* (2009a) indicated that it was unlikely to fully explain these results.] In terms of cumulative call time, all odds ratios were < 1.0 for all deciles of exposure except the highest (10th) decile (> 1640 hours). For this exposure group, the odds ratio for glioma was 1.40 (95% CI, 1.03–1.89). There were 252 cases and 253 controls who reported start of use ≥ 10 years before the reference date. The odds ratio for the highest exposure decile of cumulative call time dropped from 1.40 to 1.27 when subjects (both controls and cases) who reported use > 5 hours per day were excluded from the analysis. When mobile-phone use was truncated at 5 hours, the odds ratio was 1.38 (95% CI, 1.02–1.87). [There was reasonable doubt about the credibility of such reports and it is possible that the excess of cases in those with unreasonably high values reflected a general tendency for cases to overestimate more than controls, which could contribute to the apparent excess risk in the highest decile. As noted earlier, there is evidence that cases tended to overestimate their past exposure more than controls (Vrijheid *et al.*, 2009a).] For cases of glioma, the proportion of proxy respondents, the number of imputations for missing values, and the proportion of subjects judged by their interviewer to be non-responsive or having poor memory were all higher than for controls (INTERPHONE Study Group, 2010). However, sensitivity analyses showed that these differences by themselves did not explain the results seen in the highest decile of cumulative call time. More information on the various methodological issues and corresponding sensitivity analyses were discussed by the INTERPHONE Study Group (2010)] There was no evidence of heterogeneity in effect across study centres.

More detailed analyses were conducted by the INTERPHONE study team to evaluate the possible association between mobile-phone use and risk of glioma. The odds ratio in the highest exposure decile of cumulative use was larger for tumours in the highly exposed temporal lobe (OR, 1.87; 95% CI, 1.09–3.22) than in the less exposed parietal or frontal lobes (OR, 1.25; 95% CI, 0.81–1.91) or for tumours in other locations (OR, 0.91; 95% CI, 0.33–2.51). This result was consistent with patterns of energy deposition in the brain (Cardis *et al.*, 2008).

The ratio of the odds ratios for ipsilateral phone use to those for contralateral use increased steadily with increasing cumulative number of calls. [This would be expected if there were an exposure–response association.] However, notwithstanding similar trends in higher exposure categories, the highest ratios of these odds ratios for cumulative call time and for time since start of use were observed in the lowest exposure categories. [While these odds ratios were highly imprecise, this pattern may suggest bias in recall of side of phone use.]

In Appendix 2 of the INTERPHONE Study Group (2010) publication, an additional analysis was reported in which never-regular users were excluded from the analysis and the lowest exposure category was used as the reference category. This analysis was based on the assumption that participation bias was the principal explanation for the decreased odds ratios of the main analysis and that bias was related only to mobile-phone user status and not to extent of use. As a result,

most of the odds ratios for glioma increased above unity. Increased odds ratios were found for people who started to use their phone 2–4 years before diagnosis (OR, 1.7; 95% CI, 1.2–2.4), 5–9 years before diagnosis (OR, 1.5; 95% CI, 1.1–2.2) or > 10 years before diagnosis (OR, 2.2; 95% CI, 1.4–3.3). In terms of cumulative call time, the odds ratio for glioma did not show an upward trend for the first nine deciles of exposure, but the odds ratio for the highest category (> 1640 hours) was increased (OR, 1.8; 95% CI, 1.2–2.9).

Some publications of the results for glioma from national INTERPHONE centres were based on broader eligibility criteria, e.g. extending the age range to 20–70 years (Christensen *et al.*, 2005). Inclusion of additional cases did not yield markedly different results in these national publications compared with the pooled analysis.

[The strengths of the INTERPHONE study included its large sample size, the common core protocol, comprehensive data collection and in-depth data analyses (including a wide variety of sensitivity and validation analyses), and its use of population-based controls. The exposure assessment was, however, a limitation. As in most other case–control studies, mobile-phone use was estimated from retrospectively collected interview data and thus recall error was an issue. According to a comparison of self-reported mobile-phone use with operator-recorded data in a comparatively small sample of INTERPHONE participants from Australia, Canada and Italy, little differential exposure misclassification between cases and controls was found on average. However, in the highest category of cumulative number of calls, overestimation was more pronounced in cases than in controls (Vrijheid *et al.*, 2009a). Furthermore, the ratio of self-reported phone use to recorded phone use increased with increasing time before the interview to a greater degree in cases than in controls. Such a pattern could explain an increased risk in the most extreme exposure categories. However, the number of subjects with long-term data was relatively small and recall could only be assessed for 4–6 years at most.

Another limitation of the INTERPHONE study was the relatively low participation rate, particularly for controls (53%), which was less than that for cases (patients with glioma, 64%; meningioma, 78%; acoustic neuroma, 82%). This offered the potential for differentially selective study participation; and there is evidence that people who had ever used mobile phones regularly were more likely to agree to participate than people who had never used mobile phones regularly (Lahkola *et al.*, 2005; Vrijheid *et al.*, 2009b). This would produce downwardly biased estimates of relative risk. [The Working Group noted that a strength of this study was its use of population-based controls and the relatively high participation rate of cases.]

In summary, there was no increased risk of glioma associated with having ever been a regular user of mobile phones in the INTERPHONE study. There were suggestions of an increased risk of glioma in the group in the highest decile of exposure, for ipsilateral exposures, and for tumours of the temporal lobe [although chance, bias or confounding may explain this increased risk].

After publication of the pooled data on glioma, additional analyses were undertaken by the INTERPHONE researchers to evaluate the association between mobile-phone use and risk of glioma. They included refined dose estimation, case–case analyses, and case–specular analyses. Each of these analyses has its merits in complementing the overall picture and in evaluating the role of bias, as discussed below.

Refined dose estimation

In principle, a measure of absorbed RF radiation should be a more biologically relevant metric than "use" of mobile phones, if estimated accurately. In an attempt to derive a more biologically relevant metric, data from five INTERPHONE countries (Australia, Canada, France, Israel and

New Zealand) were used to examine the associations of tumours of the brain with RF fields from mobile phones by estimating the total cumulative specific-energy (TCSE) dose for each individual (Cardis *et al.*, 2011). For each case, the location of the tumour was determined by neuroradiologists and the centre of the tumour was estimated by a computer algorithm (Israel) or by the neuroradiologist (most participants in the other countries). This analogous tumour location was allocated to the controls matched to each case. Matching was done *post hoc* by use of an algorithm that optimized matching on interview time and age within strata defined by sex, region and, in Israel, country of birth. The number of controls per case varied from 1 to 19 (median, 3).

For each study participant, the TCSE was calculated with an algorithm considering the frequency band and communication system of all phones the subject had used, multiplied by call duration. In addition, laterality, use of hands-free devices, network characteristics and urban or rural residence were taken into account (for details, see Cardis *et al.*, 2011). A census of TCSE was carried out 1 year before the reference date.

For the glioma analysis, the 553 cases of glioma for which localization data and communication-systems information were available (42% of all eligible cases) and their 1762 controls (36% of ascertained controls) were included. Odds ratios for glioma were < 1.0 in the first four quintiles of TCSE. In the highest quintile, the odds ratio for glioma was 1.35 (95% CI, 0.96–1.90). Various sensitivity analyses did not markedly affect this odds ratio. Odds ratios in categories of TCSE were also examined in time windows since first use of a mobile phone. There was a fairly consistent dose–response pattern with an odds ratio of 1.91 (95% CI, 1.05–3.47) in the highest exposure quintile when considering TCSE exposure ≥ 7 years before the reference date. There was little evidence of an association for exposures in more recent time windows. [The Working Group noted that TCSE was highly correlated with cumulative call time (weighted kappa, 0.68). As this exposure surrogate was mainly determined by self-reported data, recall and selection bias were of concern, as they were for the other INTERPHONE analyses. Results from TCSE analyses were similar to those for cumulative duration of mobile-phone use.]

Case–case analyses

This is a novel approach for studying the effect of radiofrequency fields emitted by mobile phones. As it is based on cases only, differential participation and recall error between cases and controls is not of concern. In both studies presented below, reported preferred side of use was not considered for determining exposed brain areas. While, this should reduce the possible impact of recall bias, it probably also introduces exposure misclassification, which is expected to be random and thus would bias any risk estimates towards unity.

The same database of five countries discussed above (Cardis *et al.*, 2011) was used to conduct a case–case analysis by comparing the characteristics of mobile-phone use among people with tumours in highly exposed areas of the brain, defined as areas absorbing > 50% of the specific absorption rate (SAR) from use of mobile phones at both sides of the head (i.e. without taking into account laterality), with the corresponding characteristics of people with tumours in other parts of the brain. Comparisons were made with respect to time since first use of a mobile phone and cumulative call time. The odds ratio for presence of the tumour in the most exposed part of the brain for people who had started using a mobile-phone ≥ 10 years previously was 2.80 (95% CI, 1.13–6.94; based on 11 exposed cases), but it was not increased for people who had started using a mobile-phone more recently. There was, in addition, moderate but inconsistent evidence that the odds ratio for presence of a tumour in the most exposed area increased with increasing cumulative call time.

Data from seven INTERPHONE European countries (Denmark, Finland, Germany, Italy, Norway, Sweden, and south-eastern England) were also used to conduct a case–case analysis (Larjavaara *et al.*, 2011). In total, 888 cases of glioma in people aged between 18 and 69 years were included. For each case, the tumour midpoint on a three-dimensional grid was defined, based on radiological images. The distance to the estimated axis of a mobile phone in use on the same side of the head as the glioma was calculated, irrespective of the patient's reported typical side of phone use. Regression models were then computed to compare distance between the midpoint of the glioma and the mobile-phone axis for various exposure groups of self-reported mobile-phone use. In addition, unconditional logistic regression models were applied for the number of tumours occurring at a distance of ≤ 5 cm from the phone axis.

These analyses did not suggest an association between mobile-phone use and distance of glioma from the mobile-phone axis. For instance, the mean distance between tumour midpoint and the phone axis was similar among never-regular mobile-phone users and regular users (6.19 versus 6.29 cm; $P = 0.39$). In the dichotomized analysis examining the occurrence of tumours at a distance of ≤ 5 cm from the phone axis, odds ratios were below unity for the most exposed groups relative to never-regular users. [A limitation of the study was that exposed areas were defined on the basis of distance from the phone axis only; there were no dosimetric calculations. The results of analyses of the spatial distribution of SAR from more than 100 mobile phones (Cardis *et al.*, 2008) showed that, although there was some variability, most exposure occurs in areas of the brain closest to the ear. Exposure is not evenly distributed along the phone axis; thus the approach used could result in substantial misclassification of exposure.]

Case–specular analysis

In the case–specular analysis, a hypothetical control location is defined in the head of each patient with glioma. This was done for the data from the seven European countries described above (Larjavaara *et al.*, 2011) by symmetrically reflecting the location of the actual tumour site across the midpoint of the axial and coronal planes to obtain the mirror-image location as the control location. This counterfactual control site and the location of the actual case site were compared with respect to their distances orthogonal to the mobile-phone axis. An association would be indicated if the odds ratio increased systematically with the amount of exposure; however, this pattern was not observed. The odds ratio was larger for never-regular users than regular users. There was no increasing odds ratio for increasing use of cumulative call time.

[The strength of case–specular analysis is that each subject is his/her own control. Nevertheless, the analysis relies on self-reported use of mobile phones when comparing odds ratio between various strata. Thus exposure misclassification affects the analysis. Never-regular users were, on average, older and more commonly female, and if these factors were to affect the tumour location, bias could be introduced. However, there was little indication for this. A limitation of the study was the small number of long-term users in the case-specular analysis, resulting in wide confidence intervals. As noted above, the absence of dosimetric calculations and use of distance to the phone axis rather than to the most exposed part of the brain was a limitation.]

Hardell *et al.* (1999, 2000, 2001, 2002a, b, 2003, 2006a, b, 2009, 2010, 2011a) have published a series of papers reporting findings regarding associations between use of mobile phones and tumours of the brain. All these epidemiological analyses have been of the case–control design, with cases identified from records of regional cancer registries in Sweden and controls

identified from the Swedish population register or the Swedish death registry (the latter was used when sampling controls for deceased cases). [While reported in a series of publications, the Working Group noted that this research had involved the ongoing collection of case–control data over an extended period of time using a fixed protocol. The Working Group noted that a strength of these analyses followed from the early, and widespread, use of mobile phones in Sweden, implying a population that has accrued exposures from mobile phones over a relatively long time period (analogue phones have been in use since the early 1980s). The fairly long-term exposure from mobile phones permits consideration of any effect that may appear after a more protracted period of exposure than in other locations. Consequently, Hardell *et al.* could address higher cumulative exposures (when measured in terms of total duration of phone use), and include people using devices designed with early mobile-phone technologies, which tended to have higher power output than those based on later mobile-phone technologies.]

In the latest paper available, Hardell *et al.* (2011a) reported the findings of a pooled analysis of associations between mobile- and cordless-phone use and glioma. Cases were ascertained from 1 January 1997 to 30 June 2000 from population-based cancer registries in Uppsala-Orebro, Stockholm, Linkoping, and Gothenburg, and from 1 July 2000 to 31 December 2003 in Uppsala-Orebro and Linkoping. Eligible cases were aged 20–80 years at diagnosis. Population controls were selected from the Swedish population registry, which includes all residents; controls were matched to cases based on calendar year of diagnosis as well as age (within 5-year categories), sex and study region. Deceased controls for deceased cases were selected from the death registry. Environmental and occupational exposures were assessed by a self-administered 20-page questionnaire sent out by post. The questionnaire solicited information regarding demographic characteristics, occupational history, and other potential risk factors for cancer of the brain, and asked detailed questions on use of mobile phones and other wireless communication technologies, including year of first use, type of phone, average number of minutes of daily use, and side of head on which the phone had been used most frequently. A maximum of two reminders was sent if the questionnaire was not completed. A trained interviewer, using a structured protocol, carried out supplementary phone interviews to verify information provided in the questionnaire. Questionnaires were assigned an identification code such that the phone interviews and coding of data from questionnaires were blinded to case–control status. Study participants were asked again as to the side of head on which a phone had been used most frequently. [The Working Group noted that bias could be introduced by such an interview process; Hardell *et al.* (2002a) provided some information regarding classification of cases and controls with respect mobile-phone use based on the questionnaire, and the participants' classification after supplementary interview.] All study participants using mobile or cordless phones were sent an additional letter to re-solicit information on the side of the head on which the phone had been used most frequently. Details regarding the exposure assessment are reported in Hardell *et al.* (2006a, b). For deceased participants, an interview with a proxy (relative of the deceased) was conducted. Exposure was defined as reported use of a mobile phone and separately reported use of a cordless phone; exposure in the year immediately before case diagnosis or control selection was not included.

Cumulative lifetime use in hours was dichotomized by use of the median number of hours among controls as a cut-off point; and, lifetime use in hours was categorized into the following groups: 1–1000, 1001–2000, and ≥ 2000 hours. Three categories of time since exposure were considered > 1–5 years, > 5–10 years, and

> 10 years. Primary statistical analyses were conducted using unconditional and conditional logistic regression models with adjustment for sex, age, socioeconomic index, and year of diagnosis. Participation rates were 85% among cases and 84% among controls.

The analysis included 1148 cases with a histopathological diagnosis of glioma (Hardell *et al.*, 2011a). When mobile-phone users were compared with people who reported no use of mobile or cordless phones, or exposure > 1 year before the reference date, the odds ratio for glioma was reported to be 1.3 (95% CI, 1.1–1.6) (Table 2.13). For study participants who first used a mobile phone ≥ 10 years before the reference date, the odds ratio was 2.5 (95% CI, 1.8–3.3). This study included 123 cases of glioma and 106 controls among those who first used a mobile phone ≥ 10 years before the reference date. In terms of cumulative call time using a mobile phone, odds ratios for glioma increased with increasing categories of lifetime exposure. For the highest exposure group (> 2000 hours), the odds ratio was 3.2 (95% CI, 2.0–5.1). Use of cordless phones was also associated with glioma: the odds ratios for 1–1000 hours, 1001–2000 hours and > 2000 hours of use were 1.2 (95% CI, 0.95–1.4), 2.0 (95% CI, 1.4–3.1), and 2.2 (95% CI, 1.4–3.2), respectively. When considering age at first use, the odds ratio for mobile-phone use for all malignant tumours of the brain was 2.9 (95% CI, 1.3–6.0) for ages < 20 years, 1.3 (95% CI, 1.1–1.6) for ages 20–49 years, and 1.2 (95% CI, 1.0–1.5) for ages ≥ 50 years.

[The Working Group noted that information obtained from next of kin may be less reliable than that from living cases and controls. Analyses reported by Hardell *et al.* that are based solely on information obtained from living cases and controls are not affected by the same concerns about bias arising from information obtained from next of kin.] Excluding deceased cases (and affiliated controls) yielded odds ratios of 1.5 (95% CI, 1.1–1.9) for ever-use of analogue phones, 1.3 (95% CI, 1.1–1.6) for ever-use of digital phones, and 1.3 (95% CI, 1.1–1.6) for ever-use of cordless phones Hardell *et al.* (2006a).

Information on laterality of phone use was collected only from living cases and controls. Pooled case–control analyses were restricted to 905 living cases with malignant tumours of the brain and 2162 controls (Hardell *et al.*, 2006b; Hardell & Carlberg, 2009). Of the cases, 663 were astrocytomas (grades I–IV), 93 were oligodendrogliomas, and the remainder were other malignant tumours of the brain. Participation rates were 90% among cases with malignant tumours and 89% among controls. For users of analogue and digital mobile phones, an increased odds ratio was seen for all malignant tumours of the brain and high-grade astrocytomas with ipsilateral use of mobile phones and with the tumour on the same side of the head, but no increased risk for contralateral use of mobile phones when compared with people who had not used mobile or cordless phones (Table 2.13). [The Working Group noted that a strength of this study was its use of population-based controls and the high participation rate of cases and of controls.]

An earlier report by Hardell *et al.* included a different set of cases of tumours of the brain ascertained during 1994–96 in Uppsala and 1995–96 in Stockholm (Hardell *et al.*, 1999). Participation rates were 90% among cases and 91% among controls. The analyses included 136 cases of malignant tumours of the brain (including 48 cases of glioblastoma, 46 cases of astrocytoma, and 19 cases of oligodendroglioma), with controls matched on sex, age, and region. Of the 425 controls, 161 reported ever having used a mobile phone and 85 reported having used a mobile phone for > 136 hours. Use of a mobile phone was not associated with an increased risk of malignant tumours of the brain (OR, 1.0; 95% CI, 0.7–1.4). [The Working Group noted that a strength of the study was the high participation rates of cases and controls.]

It is useful to consider variation in effect estimates by calendar period. Among cases ascertained during 1997–2000 there were 588 malignant tumours of the brain, including 415 cases of astrocytoma and 54 cases of oligodendroglioma. Ever-use of analogue phones yielded an odds ratio of 1.13 (95% CI, 0.82–1.57), with the odds ratio for ipsilateral use being 1.85 (95% CI, 1.16–2.96) and the odds ratio for contralateral use being 0.62 (95% CI, 0.35–1.11). Ever-use of digital phones yielded an odds ratio of 1.13 (95% CI, 0.86–1.48), with an odds ratio for ipsilateral use of 1.59 (95% CI, 1.05–2.41) and an odds ratio for contralateral use of 0.86 (95% CI, 0.53–1.39) (Hardell *et al.*, 2002b).

Among cases ascertained in 2000–2003, there were 359 malignant tumours of the brain, including 248 cases of astrocytoma and 69 other malignant tumours. Ever-use of analogue phones yielded an odds ratio of 2.6 (95% CI, 1.5–4.3), with 3.1 (95% CI, 1.6–6.2) for ipsilateral use and 2.6 (95% CI,1.3–5.4) for contralateral use; and, ever-use of digital phones yielded an odds ratio of 1.9 (95% CI, 1.3–2.7) with 2.6 (95% CI, 1.6–4.1) for ipsilateral use and 1.3 (95% CI, 0.8–2.2) for contralateral use. Estimates of an association tended to be larger for use beginning > 10 years before diagnosis (Hardell *et al.*, 2006c).

(ii) Meningioma

See Table 2.14

In the case–control study of Inskip *et al.* (2001) mentioned above, interviews were conducted with a total of 197 cases of meningioma and 799 controls. Compared with non-users, self-reported regular users of mobile phones did not manifest excess risks of meningioma (OR, 0.8; 95% CI, 0.4–1.3).

The Finnish case–control study mentioned above (Auvinen *et al.*, 2002) included 129 cases of meningioma. The odds ratio for ever-use was 1.1 (95% CI, 0.5–2.4), with a slightly higher odds ratio for use of analogue phones (OR, 1.5; 95% CI, 0.6–3.5). [This study was limited by the short time since first use of a mobile phone for most people and by the uncertain mobile-phone use ascertainment from subscription information.]

In the pooled INTERPHONE analysis, 2409 cases of meningioma and 2662 controls were included (INTERPHONE Study Group, 2010). Participation rates were 78% for cases of meningioma and 53% for controls. For regular users, a reduced odds ratio was seen for cases of meningioma (OR, 0.79; 95% CI, 0.68–0.91) (see Table 2.14). Odds ratios of < 1.0 were also seen for all categories of time since start of use and for cumulative calls. Study participants who first used a mobile phone at least 10 years before interview did not show an increased risk of meningioma. Regarding cumulative number of calls, the group with highest exposure did not show an increased risk of glioma or meningioma. In terms of cumulative call time, all odds ratios were < 1.0 for all deciles of exposure except the highest (10th) decile of recalled cumulative call time (≥ 1640 hours). For this exposure group, the odds ratio for meningioma was 1.15 (95% CI, 0.81–1.62). Increased risk in the highest exposure decile of cumulative call time was more pronounced in short-term users, who started to use phones 1–4 years before the reference date, than in long-term users (≥ 10 years). Sensitivity analyses had little effect on estimated associations between mobile-phone use and risk of meningioma.

The analysis of TCSE and risk of meningioma in five INTERPHONE countries (Cardis *et al.*, 2011) was based on 674 cases of meningioma and 1796 controls. In the highest quintile of TCSE, the odds ratio for meningioma was 0.90 (95% CI, 0.66–1.24). An odds ratio of 1.01 (95% CI, 0.75–1.36) was reported for the highest quintile of cumulative call time without hands-free devices. In terms of TCSE exposure ≥ 7 years before the reference date, there was no consistent dose–response pattern, but the odds ratio was elevated in the quintile of highest exposure (OR, 2.01; 95% CI, 1.03–3.93). In case-only analyses, the

Table 2.14 Case–control studies of meningioma and use of mobile phones

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (1999) Sweden, 1994–96	46	439	Population, matched on sex, age, region, and year of diagnosis	Self-administered standardized questionnaire	Meningioma	Never use of mobile phone	30	1.0		
						Ever use	16	1.0 (0.5–2.3)		
Inskip *et al.* (2001) Phoenix, Boston, Pittsburgh, 1994–98.	197	799	Patients admitted to the same hospitals for a variety of non-malignant conditions.	Computer-assisted, personal interview in the hospital	Meningioma	Regular use	32	0.8 (0.4–1.3)	Hospital, age, sex, race or ethnic group, proximity of residence to the hospital	There are results for other exposure metrics: average daily use, duration, year use began. Also results for laterality.
						Duration ≥ 5 yr	6	0.9 (0.3–2.7)		
						Cumulative use (h)				
						Never or rarely used	165	1.0		
						< 13	8	0.7 (0.3–1.9)		
						13–100	13	1.1 (0.5–2.4)		
						> 100	11	0.7 (0.3–1.7)		
						> 500	6	0.7 (0.2–2.4)		
Auvinen *et al.* (2002) Finland, 1996	398 (129 meningiomas)	1990	Population Registry Centre of Finland	Information on subscriptions obtained from the two mobile-network providers operating in Finland in 1996	Meningioma (225.2)	*Analogue*			Age, sex	Cases aged 20–69 yr
						Ever	8	1.5 (0.6–3.5)		
						< 1 yr	3	2.3 (0.6–9.2)		
						1–2 yr	3	1.6 (0.4–6.1)		
						> 2 yr	2	1.0 (0.2–4.4)		
						Digital				
						Ever	3	0.7 (0.2–2.6)		

Table 2.14 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2006a) Sweden, 1997–2003	916	2162	Population.	Self-administered questionnaire	Meningioma	Never used mobile or cordless phone	455	1.0	Age, sex, SEI, year of diagnosis	Ipsilateral use of analogue and digital phones was associated with meningioma (analogue: OR, 1.3; 95% CI, 0.9–2.0; digital: OR, 1.4; 95% CI, 1.0–1.8), contralateral use was not (OR, 1.2; 95% CI, 0.7–1.8; and OR, 1.1; 95% CI, 0.8–1.5, respectively).
						Cumulative use, analogue (h)				
						1–500	99	1.3 (1.0–1.7)		
						501–1000	8	1.1 (0.5–2.6)		
						> 1000	6	1.4 (0.5–3.8)		
						Cumulative use, digital (h)				
						1–500	268	1.1 (0.9–1.3)		
						501–1000	18	1.0 (0.6–1.8)		
						> 1000	9	0.7 (0.3–1.4)		
						Latency, analogue (yr)				
						> 1–5	32	1.2 (0.8–1.8)		
						> 5–10	47	1.2 (0.8–1.8)		
						> 10	34	1.6 (1.0–2.5)		

Table 2.14 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
INTERPHONE Study Group (2010) Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, United Kingdom, 2000–04	2409	2662	Population (except United Kingdom: GP patients)	Interviewer-administered standardized questionnaire	Meningioma (D32.0, D32.9, D42.0, D42.9, C70.0, C70.9)	Never regular use of mobile phone	1147	1.00	Sex, age, study centre, ethnicity (in Israel), and education	
						Ever use	1262	0.79 (0.68–0.91)		
						Time since start of use (yr)				
						1–1.9	178	0.90 (0.68–1.18)		
						2–4	557	0.77 (0.65–0.92)		
						5–9	417	0.76 (0.63–0.93)		
						≥ 10	110	0.83 (0.61–1.14)		
						Cumulative call time with no hands-free devices (h)				OR, 4.80 (95% CI, 1.49–15.4) in short-term users (start of mobile-phone use 1–4 yr before reference date) with cumulative call time ≥ 1640 h (based on 22 cases)
						< 5	160	0.90 (0.69–1.18)		
						5–12.9	142	0.82 (0.61–1.10)		
						13–30.9	144	0.69 (0.52–0.91)		
						31–60.9	122	0.69 (0.51–0.94)		
						61–114.9	129	0.75 (0.55–1.00)		
						115–199.9	96	0.69 (0.50–0.96)		
						200–359.9	108	0.71 (0.51–0.98)		
						360–734.9	123	0.90 (0.66–1.23)		
						735–1639.9	108	0.76 (0.54–1.08)		
						≥ 1 640	130	1.15 (0.81–1.62)		

Table 2.14 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Cardis *et al.* (2011) Australia, Canada, France, Israel, Italy, New Zealand, 2000–04	674	1796	Population	Interviewer-administered standardized questionnaire	Meningioma	*RF TCSE (J/kg)*			Sex, age, study centre, ethnicity (in Israel) and education	Interpretation of OR is most meaningful when compared with the corresponding OR for comparable exposure surrogates of mobile-phone use
						Never regular user	294	1.0		Subjects with tumour centre estimated by a neuro-radiologist or by means of a computer algorithm
						< 76.7	103	0.90 (0.67–1.21)		
						76.7-	71	0.74 (0.53–1.04)		Exposure ≥ 7 yr before reference date: OR, 2.01 (95% CI, 1.03–3.93), for highest quintile
						284.1-	56	0.56 (0.39–0.80)		
						978.9-	62	0.72 (0.51–1.02)		
						3123.9+	88	0.90 (0.66 to 1.24)		

h, hour; OR, odds ratio; RF, radiofrequency radiation; SEI, socioeconomic index; TCSE, total cumulative specific energy; yr, year

odds ratio for having the centre of the tumour within the most exposed area was 1.34 (95% CI, 0.55–3.25) in those who reported starting to use a mobile phone ≥ 10 years previously.

Hardell *et al.* (2006a) reported the results of a pooled analysis of case–control studies of benign tumours of the brain and use of mobile and cordless phones that included 1254 cases of benign tumours, of which 916 were meningioma; deceased cases (and controls) were not included in this analysis. An odds ratio of 1.3 (95% CI, 0.99–1.7) was reported for meningioma when users of analogue mobile phones were compared with people who reported no use of mobile or cordless phones, or exposure ≤ 1 year before the reference date. The odds ratio was 1.1 (95% CI, 0.9–1.3) for users of digital mobile phones and 1.1 (95% CI, 0.9–1.4) for users of cordless phones. Study participants who first used an analogue, digital, or cordless phone at least 10 years previously showed increased risks of meningioma, although estimates were imprecise (OR, 1.6; 95% CI, 1.0–2.5; OR, 1.3; 95% CI, 0.5–3.2; OR, 1.6; 95% CI, 0.9–2.8, respectively).

(iii) Acoustic neuroma

See Table 2.15

Inskip *et al.* (2001) included a total of 96 cases with acoustic neuroma and 799 controls. Compared with non-users, self-reported regular users of mobile phones did not manifest excess risks of acoustic neuroma (OR, 1.0; 95% CI, 0.5–1.9).

A case–control study of 90 cases of acoustic neuroma and 86 controls selected from among other patients was conducted in a hospital in New York (Muscat *et al.*, 2002). Subjects were interviewed regarding use of mobile phones and other factors. Analysis of reported histories of mobile-phone use, adjusting for sociodemographic factors and date of interview, yielded a set of odds-ratio estimates that were close to the null value for cumulative hours of use and years of use. [The Working Group noted that numbers were small, exposure levels were low, and time since first use was short.]

Schoemaker *et al.* (2005) reported pooled results on acoustic neuroma from a subset of the INTERPHONE countries (the five north European countries: Denmark, Finland, Norway, Sweden, and the United Kingdom). There was no indication of an increased risk of acoustic neuroma associated with mobile-phone use (Table 2.15). Similar negative findings were reported by the INTERPHONE groups in France (Hours *et al.*, 2007) and Germany (Schlehofer *et al.*, 2007), and from a case–control study in Japan (Takebayashi *et al.*, 2006).

In Japan, Sato *et al.* (2011) identified a series of cases of acoustic neuroma diagnosed between 2000 and 2006 in 22 participating hospitals with neurosurgery departments (32% of hospitals solicited). Of 1589 cases identified, 816 agreed to respond to a self-administered questionnaire, received by post, focusing on history of mobile-phone use and history of pre-diagnosis symptoms. Two case series were constituted consisting of: (a) 180 cases among mobile-phone users whose symptoms had not appeared 1 year before diagnosis; and (b) 150 cases among mobile-phone users whose symptoms had not yet appeared 5 years before diagnosis. In each series, the investigators then compared laterality of the tumour with laterality of mobile-phone use and, using a formula described by Inskip *et al.* (2001), they derived an estimate of relative risk of acoustic neuroma related to various metrics of mobile-phone use. Overall, there was no excess risk of acoustic neuroma among ever-users of mobile phones. However, among some subgroups, namely those with the highest duration of daily calls, there were estimates of high risk ratios in the range of 2.74 (95% CI, 1.18–7.85) to 3.08 (95% CI, 1.47–7.41). This excess appeared to be restricted to a small group of cases who were persistently among the highest users during the past 5 years. The authors considered various alternative explanations for this finding,

Table 2.15 Case–control studies of acoustic neuroma and use of mobile phones

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Inskip *et al.* (2001) USA, 1994–98	96	799	Patients admitted to the same hospitals for a variety of non-malignant conditions	Computer-assisted personal interview in the hospital	Acoustic neuroma	Regular use Duration ≥ 5 yr	22 5	1.0 (0.5–1.9) 1.9 (0.6–5.9)	Hospital, age, sex, race or ethnic group, proximity of residence to the hospital	Analyses by cumulative use showed no associations. Analyses of laterality of tumour by laterality of phone use showed no associations. Very few subjects with long-term exposure. Response rates were 92% for cases and 86% for controls. In groups with highest duration of daily calls: RR ranged from 2.74 (95% CI, 1.18–7.85) to 3.08 (95% CI, 1.47–7.41)
Muscat *et al.* (2002) New York City, 1997–99	90	86	In-patients with non-malignant conditions from the same hospitals	Interviews with structured questionnaire	Acoustic neuroma (225.1)	Cumulative use (h): 0 1–60 > 60 Years of use: 0 1–2 3–6	 72 9 9 72 7 11	 1.0 0.9 (0.3–3.1) 0.7 (0.2–2.6) 1.0 0.5 (0.2–1.3) 1.7 (0.5–5.1)	Age, education, sex, study centre, occupation categories, and date of interview	Also presented as h/mo, with similar results. In mobile-phone users tumour was most often on contralateral side.

Table 2.15 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Schoemaker *et al.* (2005) Denmark, Finland, Norway, Sweden, United Kingdom, 1999–2004	678	3553	Population (except United Kingdom: GP patients)	Interviewer-administered standardized questionnaire	Acoustic neuroma (D33.3)	Never regular use of mobile phone	316	1.0	Educational level and combinations of interview year and interview lag time	Matched for centre, region, 5-yr age group, sex
						Regular use	360	0.9 (0.7–1.1)		
						Time since start of use (yr)				
						1.5–4	174	0.8 (0.7–1.0)		
						5–9	139	0.9 (0.7–1.2)		
						≥ 10	47	1.0 (0.7–1.5)		
						P for trend		0.9		
						Cumulative use (h)				
						< 116	168	0.9 (0.7–1.1)		
						116–534	89	0.9 (0.7–1.2)		
						> 534	94	0.9 (0.7–1.2)		
						P for trend		0.5		
Takebayashi *et al.* (2006) Japan, 2000–04	101	339	Population (random-digit dialling)	Interviewer-administered standardized questionnaire	Acoustic neuroma (D33.3)	Never regular use of mobile phone	46	1.0	Education, marital status	Matched for age, sex, residency
						Regular use	51	0.73 (0.43–1.23)		
						Time since start of use (yr)				
						< 4	26	0.70 (0.39–1.27)		
						4–7	21	0.76 (0.38–1.53)		
						≥ 8	4	0.79 (0.24–2.65)		
						P for trend		0.70		
						Cumulative use (h)				
						< 300	35	0.67 (0.38–1.17)		
						300–900	9	1.37 (0.54–3.50)		
						> 900	7	0.67 (0.25–1.83)		
						P for trend		0.69		

Table 2.15 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Ha *et al.* (2007) France, 2001–03	109	214	Population (electoral rolls)	Interviewer-administered standardized questionnaire	Acoustic neuroma (D33.3)	Never regular use of mobile phone	51	1.0	SES, tobacco consumption, noise exposure	Sex, age (± 5 yr), place of residence
						Regular use	58	0.92 (0.53–1.59)		
						Duration of use (mo)				
						< 16	19	1.21 (0.55–2.69)		
						16–27	17	1.33 (0.58–3.03)		
						27–46	8	0.63 (0.26–1.53)		
						> 46	14	0.66 (0.28–1.57)	OR per 1 year, 0.96 (0.84–1.10)	
						Cumulative use (h)				
						< 20	14	1.06 (0.48–2.36)		
						20–80	15	0.87 (0.40–1.91)		
						80–260	13	0.85 (0.38–1.88)		
						> 260	16	0.92 (0.41–2.07)	OR per 80 h, 1.0 (0.96–1.03)	
Schlehofer *et al.* (2007) Germany, 1976–88	97	194	Population	Interviewer-administered standardized questionnaire	Acoustic neuroma (D33.3)	Never regular use of mobile phone	68	1.0	SES, urbanity	Matched for centre, age, sex
						Regular use	29	0.67 (0.38–1.19)		
						Time since start of use (yr)				
						1–4	20	0.78 (0.40–1.50)		
						5–9	8	0.53 (0.22–1.27)		
						≥ 10	0	-		
						Cumulative use (h)				
						< 44	16	1.04 (0.51–2.16)		
						44–195	7	0.58 (0.22–1.48)		
						> 195	5	0.35 (0.12–1.01)		

Table 2.15 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Sato *et al.* (2011) Japan, 2000–06	787	787 (case–case)	Note: the affected ear is the case side; the opposite ear is regarded as the control.	Mailed questionnaire about history of mobile-phone use	Acoustic neuroma	Overall, for regular mobile-phone use until one yr before diagnosis	180	1.08 (0.93–1.28)	Same patients	The authors interpret these significant results with caution, mentioning detection and recall bias as possibilities.
						Overall, for regular mobile-phone use until 5 yr before diagnosis	150	1.14 (0.96–1.40)		
						Weighted daily average call duration > 20 min, 1 yr before diagnosis	23	2.74 (1.18–7.85)		
						Weighted daily average call duration > 20 min, 5 yr before diagnosis	33	3.08 (1.47–7.41)		

Table 2.15 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
INTERPHONE Study Group (2011) Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, United Kingdom, 2000–04	1105	2145	Population (except United Kingdom: GP patients)	Interviewer-administered standardized questionnaire	Schwannoma of the acoustic nerve (ICD-9 code 225.1 or ICD-10 code D33.3, and ICD-O topography code C72.4 and morphology code 9560/0)	Never regular use of mobile phone	801	1.00	Sex, age, study centre, ethnicity (in Israel), and education	Data are given only for exposure up to 5 yr before reference date (risk estimates were generally smaller when exposure up to 1 yr before reference date was considered)
						Regular use	304	0.95 (0.77–1.17)		
						Time since start of use (yr)				
						5–9	236	0.99 (0.78–1.24)		
						≥ 10	68	0.83 (0.58–1.19)		
						Cumulative call time (h) with no hands-free devices				When stratifying for duration of use, OR was highest in long-term users (start of mobile-phone use ≥ 10 yr ago): OR, 1.93 (95% CI, 1.10–3.38). Ipsilateral use: OR, 3.74 (95% CI, 1.58–8.83); contralateral use: OR, 0.48 (95% CI, 0.12–1.94)
						< 5	42	1.07 (0.69–1.68)		
						5–12.9	30	1.06 (0.60–1.87)		
						13–30.9	40	1.32 (0.80–2.19)		
						31–60.9	36	0.86 (0.52–1.41)		
						61–114.9	21	0.63 (0.35–1.13)		
						115–199.9	22	0.71 (0.39–1.29)		
						200–359.9	49	0.83 (0.48–1.46)		
						360–734.9	26	0.74 (0.42–1.28)		
						735–1639.9	22	0.60 (0.34–1.06)		
						≥ 1640	32	2.79 (1.51–5.16)		

Table 2.15 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2006a) Sweden, 2000–03	243		Population	Self-administered standardized questionnaire	Acoustic neuroma	Never use of mobile or cordless phone	88	1.0	Age, sex, SEI, and year of diagnosis	
						Ever use of analogue phone	68	2.9 (2.0–4.3)		
						Ever use of digital phone	105	1.5 (1.1–2.1)		
						Ever use of cordless phone	96	1.5 (1.0–2.0)		
						Cumulative call time, analogue (h)				
						1–500	55	2.8 (1.8–4.2)		
						501–1000	7	3.3 (1.3–8.0)		
						> 1000	6	5.1 (1.9–14)		
						Cumulative call time, digital (h)				
						1–500	83	1.4 (1.0–2.0)		Users of analogue phone (> 10 yr) showed OR, 3.1 (95% CI, 1.7–5.7)
						501–1000	10	1.8 (0.8–3.8)		
						> 1000	12	3.1 (1.5–6.4)		
						Cumulative call time, cordless (h)				
						1–500	60	1.3 (0.9–1.9)		
						501–1000	15	1.6 (0.9–3.0)		
						> 1000	21	2.1 (1.2–3.7)		

GP, general practitioner; h, hour; min, minute; mo, month; OR, odds ratio; SEI, socioeconomic index; SES, socioeconomic status; yr, year

including selection bias and recall bias, and they concluded that it was unclear whether the finding was a consequence of bias.

The pooled INTERPHONE analysis for acoustic neuroma (INTERPHONE Study Group, 2011) followed in general the same methodology as the analyses for glioma and meningioma described above (INTERPHONE Study Group, 2010). Patients diagnosed with a schwannoma of the acoustic nerve in the study regions during study periods of 2–4 years between 2000 and 2004 were included in the study. For each case, two age-, sex- and study-region-matched controls were recruited. Controls were either specifically sampled for the cases of acoustic neuroma, taken from the pool of INTERPHONE controls drawn for all tumours together, or obtained with a combination of both approaches. In total, 1105 cases (participation rate, 82%) were included in the analyses, together with 2145 controls (participation rate, 53%). The odds ratio for regular use was 0.85 (95% CI, 0.69–1.04) when recording exposure at 1 year before the reference date and 0.95 (95% CI, 0.77–1.17) when recording exposure at 5 years before the reference date. For cumulative call time, the highest odds ratios were observed in the highest category of use: the odds ratios for ≥ 1640 hours were 1.32 (95% CI, 0.88–1.97) when recording exposure at 1 year and 2.79 (95% CI, 1.51–5.16) when recording exposure at 5 years. There was, however, no consistent trend in the exposure–response relationship in the first nine deciles of exposure. Stratifying the analyses according to time since start of mobile-phone use resulted in an increased odds ratio for heavy users of mobile phones only in long-term users (OR, 1.93; 95% CI, 1.10–3.38, based on 37 cases). This risk estimate was more pronounced with respect to ipsilateral use (OR, 3.74; 95% CI, 1.58–8.83, based on 28 cases) and decreased with respect to contralateral use (OR, 0.48; 95% CI, 0.12–1.94, based on 4 cases). Exclusion of participants with an implausible amount of use (> 5hours per day) resulted in a decrease in odds ratio for exposure up to 1 year before the reference date, but had little impact on the results of the analyses of exposure up to 5 years before the reference date. The results for cumulative number of calls were broadly similar, but risk estimates were smaller.

Overall, these results were broadly similar to the results for glioma from the INTERPHONE study. [The same methodological limitations were of concern, mainly selection and recall bias. Diagnostic bias was also of concern: patients with acoustic neuroma who use mobile phones may be diagnosed earlier than non-users, since acoustic neuroma affects hearing capability. However, such an effect would be expected to be most relevant for recent users, but of little relevance for exposure 5 years before diagnosis. On the other hand, prodromal symptoms might discourage cases from becoming mobile-phone users. Again, such an effect would be most relevant in the analysis of most recent use of mobile phones, but not in the analysis of exposure at earlier dates. There is also uncertainty as to how early symptoms may affect the preferred side of use. Regarding confounding, socioeconomic status, ionizing radiation and loud noise were considered, with little effect on the results.]

Hardell *et al.* (2006a) reported the results of a pooled analysis of associations between use of mobile and cordless phones and risk of benign tumours of the brain that included 243 cases of acoustic neuroma. An increased odds ratio was reported for acoustic neuroma (OR, 2.9; 95% CI, 2.0–4.3) when users of analogue mobile phones were compared with people who reported no use of mobile or cordless phones, or exposure ≤ 1 year before the reference date. The odds ratio was 1.5 (95% CI, 1.1–2.1) for users of digital mobile phones and 1.5 (95% CI, 1.04–2.0) for users of cordless phones. Study participants who first used an analogue phone at least 10 years before the reference date showed increased risks (OR, 3.1; 95% CI, 1.7–5.7), but users of digital or cordless phones did not. For users of analogue mobile phones, an increased odds ratio was

seen for ipsilateral use (OR, 3.0; 95% CI, 1.9–5.0) and contralateral use (OR, 2.4; 95% CI, 1.4–4.2) when compared with people who had not used mobile or cordless phones. For users of digital mobile phones, an increased odds ratio was seen for acoustic neuroma with ipsilateral use (OR, 1.7; 95% CI, 1.1–2.6), but not for contralateral use (OR, 1.3; 95% CI, 0.8–2.0) when compared with people who had not used mobile or cordless phones. Similar associations were found for use of cordless phones (ipsilateral use: OR, 1.7; 95% CI, 1.1–2.6; and contralateral use: OR, 1.1; 95% CI, 0.7–1.7, respectively) (Schüz *et al.*, 2006c).

(iv) All cancers of the brain combined

See Table 2.16

In several studies already referred to above, analyses were presented for all cancers of the brain combined (Hardell *et al.*, 2000, 2001, 2011a; Inskip *et al.*, 2001; Auvinen *et al.*, 2002). Only in Hardell *et al.* (2011a) were risks of cancer significantly elevated with prolonged use of mobile phones. A study in France by Spinelli *et al.* (2010) found no significant excess risks.

(v) Other cancers of the brain

A pooled analysis by Hardell *et al.* (2011a) included 103 cases with a histopathological diagnosis of malignant tumour of the brain other than glioma. Odds ratios for malignant tumours other than glioma by category of duration of mobile-phone use were 1.0 (95% CI, 0.6–1.6) for 1–1000 hours, 1.4 (95% CI, 0.4–4.8) for 1001–2000 hours, and 1.2 (95% CI, 0.3–4.4) for > 2000 hours.

(vi) Pituitary tumours

See Table 2.17

In a Japanese study, 102 cases of pituitary adenoma were included, together with 161 individually matched controls (Takebayashi *et al.*, 2008). Neither regular use of mobile phones (OR, 0.90; 95% CI, 0.50–1.61) nor cumulative duration of use in years and cumulative call time in hours was associated with an increased risk of pituitary tumours.

In a population-based case–control study from south-eastern England, 291 cases of pituitary tumour diagnosed between 2001 and 2005 were included, together with 630 controls that were frequency-matched for sex, age, and health-authority of residence (Schoemaker & Swerdlow, 2009). The participation rate was 63% for cases and 43% for controls. Data were collected with a face-to-face interview at the subject's home or another convenient place. Regular use was not associated with an increased risk (OR, 0.9; 95% CI, 0.7–1.3) nor was any other exposure surrogate. Stratified analyses for analogue or digital mobile-phone user did not indicate consistent exposure–response associations.

(d) Some reviews, meta-analyses, and other studies

Various meta-analyses and other comparisons of the accumulating data on mobile-phone use and tumours of the brain have been published (Hardell *et al.*, 2003, 2007a, 2008; Lahkola *et al.*, 2006; Kan *et al.*, 2008; Ahlbom *et al.*, 2009; Hardell & Carlberg, 2009; Khurana *et al.*, 2009; Myung *et al.*, 2009). Such analyses are potentially useful for characterizing the accumulating evidence and for exploring heterogeneity of findings among studies, along with determinants of any observed heterogeneity. [The Working Group based its conclusions on review of the primary studies.]

2.3.2 Leukaemia and lymphoma

(a) Leukaemia

There have been four epidemiological studies on leukaemia and use of mobile phones.

In an early cohort study of 285 561 users of analogue phones, identified based on records from two mobile-phone providers in the USA in 1993, mortality attributable to leukaemia was not elevated among users of hand-held phones relative to users of non-hand-held phones (mostly car phones) (Dreyer *et al.*, 1999; Table 2.18). [A

Table 2.16 Case–control studies of all cancers of the brain and use of mobile phones

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2000, 2001) Uppsala-Orebro region and Stockholm region, Sweden, 1994–96	209 cases of brain tumours diagnosed 1994–96 among people aged 20–80 yr at diagnosis	425	Population register. 1:2 case:control ratio with matching on age and sex, and drawn from the same geographical areas as the cases	Self-administered structured, mailed questionnaire	All malignant tumours of the brain. Benign tumours of the brain included from Stockholm in 1996, as part of feasibility study. Histopathology reports on 197 patients, 136 with malignant and 62 with benign tumours.	No use of mobile or cordless phone, or exposure ≤ 1 yr before reference date Mobile-phone use	 78	1 0.98 (0.69–1.41)	Sex, age (as a continuous variable). Radiotherapy, diagnostic X-ray, asbestos, solvents, smoking	Participation rate was 90% for cases and 91% for controls. Increased risk for tumour in the temporal or occipital lobe on same side as cell-phone use (OR, 2.62; 95% CI, 1.02–6.71). Contralateral use did not increase the risk (OR, 0.97; 95% CI, 0.36–2.59). Deceased cases were not included. This analysis encompassed the case–control data included in Hardell *et al.* (2000)
Inskip *et al.* (2001) USA, 1994–98	782	799	Patients admitted to the same hospitals for a variety of non-malignant conditions.	Computer-assisted in person interview in the hospital, history of mobile-phone use	All brain	No use Regular use Duration ≥ 5 yr	471 139 22	1.0 0.8 (0.6–1.1) 0.9 (0.5–1.6)	Hospital, age, sex, race or ethnic group, proximity of residence to the hospital	Analyses by cumulative use showed no associations. Very few subjects with long-term exposure. Response rates 92% for cases and 86% for controls.

Table 2.16 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Auvinen *et al.* (2002) Finland, 1996	398	1990	Population Registry Centre of Finland	Information on subscriptions obtained from the two mobile-network providers operating in Finland in 1996	All brain (191 and 225.2)	*Analogue*			Age, sex	Cases aged 20–69 yr
						Ever	40	1.6 (1.1–2.3)		
						< 1 yr	8	1.6 (0.7–3.6)		
						1–2 yr	15	1.5 (0.9–2.8)		
						> 2 yr	17	1.6 (0.9–2.8)		
						Digital				
						Ever	16	0.9 (0.5–1.5)		
						< 1 yr	4	0.6 (0.2–1.6)		
						1–2 yr	11	1.2 (0.6–2.3)		
						> 2 yr	1	0.6 (0.1–4.5)		
Spinelli *et al.* (2010) France, 2005	122	122	In-patients from neurosurgery departments of the same hospitals; unrelated to cancer	Face-to-face interviews with standardized questionnaire; and self-administered questionnaire	Malignant primary tumours of the brain	*Global cellular-phone use (hours-year)*			Age, sex	
						0	37	1		
						≤ 4	8	0.86 (0.30–2.44)		
						4–36	58	1.45 (0.75–2.80)		
						≥ 36	13	1.07 (0.41–2.82)		

Table 2.16 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2011a)	1251 cases of malignant brain tumours diagnosed during 1997–2003 among people aged 20–80 yr at diagnosis	2438 controls	Population register. 1:1 case:control ratio with matching on age and sex, and drawn from the same region as the cases. For deceased cases, controls drawn from death registry. 1:1 matching on year of death, sex, age, and medical region	Self-administered structured, mailed questionnaire. For deceased cases and controls, mailed questionnaire was completed by relative of decedent.	All malignant tumours of the brain	No use of mobile or cordless phone, or exposure ≤ 1 yr before reference date	677	1.00	Sex, age (as a continuous variable), SEI code, year of diagnosis	Participation rates were 85% for cases and 84% for controls. This analysis encompassed the data presented in earlier papers on pooled case–control studies of malignant tumours of the brain among living cases diagnosed in 1997–2003
						Mobile-phone use:				
						Ever	574	1.3 (1.1–1.5)		
						1–1000 h	466	1.2 (1.0–1.4)		
						1001–2000 h	47	1.8 (1.1–2.7)		
						> 2000 h	61	3.0 (1.9–4.8)		
					Malignant tumours of the brain other than glioma (*n* = 103)	Mobile-phone use:				
						1–1000 h	39	1.0 (0.6–1.6)		
						1001–2000 h	3	1.4 (0.4–4.8)		
						> 2000 h	3	1.2 (0.3–4.4)		

h, hour or hours; SEI, socioeconomic index; yr, year

Table 2.17 Case–control studies of cancers of the pituitary and use of mobile phones

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Takebayashi *et al.* (2008) Japan, 2000–04	101	161	Population (random-digit dialling)	Interviewer-administered standardized questionnaire	Pituitary adenoma (ICD code not reported)	Never regular use of mobile phone	39	1.0	Education, marital status	Matched for age (5 yr), sex, residency
						Regular use	62	0.90 (0.50–1.61)		
						Time since start of use (yr)				
						< 2.2	14	0.86 (0.39–1.88)		
						2.2–4.69	13	0.75 (0.31–1.81)		
						4.7–6.5	22	1.64 (0.74–3.66)		
						> 6.5	13	0.75 (0.31–1.82)		
						P for trend		0.89		
						Cumulative use (h)				
						< 39	15	1.00 (0.46–2.16)		
						39–190	14	0.97 (0.40–2.32)		
						190–560	12	0.72 (0.31–1.70)		
						> 560	21	1.33 (0.58–3.09)		
Schoemaker & Swerdlow (2009) United Kingdom, 2001–05	291	630	Population (from GP patient list)	Interviewer-administered standardized questionnaire	Pituitary tumour (C75.1, D35.2, D44.3)	Never regular use of mobile phone	116	1.0	Age, sex, category, geographic area, reference date, and Townsend deprivation score	
						Regular use	175	0.9 (0.7–1.3)		
						Time since start of use (yr)				
						1.5–4	89	1.0 (0.7–15)		
						5–9	62	0.8 (0.5–1.2)		
						10–17	24	1.0 (0.5–1.9)		
						P for trend		0.7		
						Cumulative use (h)				
						< 113	79	0.9 (0.6–1.3)		
						113–596	44	1.1 (0.7–1.8)		
						> 596	51	1.1 (0.7–1.7)		
						P for trend		0.9		

GP, general practitioner; h, hour or hours; yr, year

limitation of this study was that there were only four deaths due to leukaemia among users of hand-held phones, as the study was truncated – with no access to mortality data beyond 1 year – as a result of a legal proceeding.]

A study of cancer incidence in a cohort of 420 095 users of mobile phones in Denmark found no evidence of an elevated risk of leukaemia in males or females (SIR, 1.05; 95% CI, 0.96–1.15) (Schüz *et al.*, 2006c; Table 2.18). The incidence of leukaemia was not increased in any of the reported time intervals since first subscription. Details concerning the design of the study were discussed above (Section 2.3.1). [The results for leukaemia were not reported separately by subtype.]

A hospital-based case–control study of adult-onset leukaemia in Thailand conducted between 1997 and 2003 (180 cases, 756 hospital controls) reported an odds ratio for all leukaemias combined of 1.5 (95% CI, 1.0–2.4) (Kaufman *et al.*, 2009; Table 2.19). Overall, the duration of mobile-phone use was short (median, 24–26 months). The results were similar for acute myeloid leukaemia, chronic myeloid leukaemia and chronic lymphocytic leukaemia. There were no trends in associations of all leukaemias with duration of ownership, lifetime hours of use, or amount of use per year. The odds ratio was highest for persons reporting exclusive use of GSM (Global System for Mobile Communications) services. Using an categorization ad hoc into "high risk" and "low risk" groups of mobile-phone users based on phone characteristics, the authors reported an odds ratio of 1.8 for high-risk versus low-risk users (95% CI, 1.1–3.2). [It was unclear to the Working Group as to how the "high risk" and "low risk" groups were derived and whether it was done *a priori* or *a posteriori*.]

In a study conducted in the United Kingdom between 2003 and 2009, which included 806 cases and 585 controls who were non-blood relatives, regular use of a mobile phone (defined as at least one call per week for at least 6 months) was not associated with the incidence of leukaemia (Cooke *et al.*, 2010; Table 2.19). Risk was not significantly associated with years since first use, lifetime years of use, cumulative number of calls, or cumulative hours of use. Among people who reported using a phone for ≥ 15 years since first use, the odds ratio was 1.87 (95% CI, 0.96–3.63; 50 exposed cases); however, there was no apparent trend with years since first use. There also was no apparent trend in risk with cumulative hours of use. Findings were similar for digital and analogue phones. There was no apparent variation in results by subtype of leukaemia and no trend in risk with years since first use, years of use, or cumulative hours of use for any subtype. [Only 50% of potential cases participated, with the usual reasons for non-participation being death or disability related to leukaemia.]

(b) Lymphoma

In a population-based case–control study conducted in Sweden between 1999 and 2002 (910 cases, 1016 controls), neither mobile-phone use nor cordless-phone use was significantly associated with risk of NHL overall, nor for the B-cell subtype in particular (90% of the cases) (Hardell *et al.*, 2005; Table 2.19). High odds ratios were reported for some categories of use of cordless phones for T-cell lymphomas, based on very small numbers. Cases in this study were diagnosed between the ages of 18 and 74 years. Males and females were included, but the main results concerning mobile-phone use were presented for both sexes combined.

A population-based case–control study of NHL conducted in the USA between 1998 and 2000 (551 cases, 462 controls) also reported predominantly null findings (Linet *et al.*, 2006; Table 2.19). Several exposure metrics of mobile-phone use were presented (latency, duration, amount of exposure), but overall there was no consistent trend in risk. Risk of NHL was not associated with minutes per week of use of mobile telephones, duration of use, cumulative

Table 2.18 Cohort studies of leukaemia, lymphoma, and other cancers, and use of mobile phones

Reference, study location and period	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Dreyer *et al.* (1999) USA, 1993	285 561	1993	Records of mobile-phone service providers	Leukaemia (204–207)	*Hand-held phones* < 2 min/d ≥ 2 min/d	 2 2	*SMR* 1.6 4.9	Age, sex, metropolitan area	Mortality study; effect estimate = SMR; SMR for non-hand-held phones (non-exposed), 7.0
Schüz *et al.* (2006c) Denmark, 1982–2002	420 095	1982–2002	Records of mobile-phone service providers	Leukaemia (204–207)	*Latency (yr)* < 1 1–4 5–9 ≥ 10	 33 151 135 32	*SIR* 1.09 (0.75–1.52) 1.05 (0.90–1.24) 0.92 (0.77–1.08) 1.08 (0.74–1.52)	Age, sex, calendar period of observation	Incidence study; cannot be certain who the user was; phones used under business accounts not included; details of phone use not available
Schüz *et al.* (2006c) Denmark, 1982–2002	65 542	1982–2002	Records of cellular service providers	Female breast (174)	Subscriber	711	1.04 (0.97–1.12)	Age, calendar year of observation	Incidence study; cannot be certain who the user was; phones used under business accounts not included; details of phone use not available
Schüz *et al.* (2006c) Denmark, 1982–2002	420 095	1982–2002	Records of cellular service providers	Eye (190)	Subscriber	38 (males) 6 (females)	0.94 (0.66–1.29) 1.10 (0.40–2.39)	Age, calendar year of observation	Incidence study; cannot be certain who the user was; phones used under business accounts not included; details of phone use not available

Table 2.18 (continued)

Reference, study location and period	Total No. of subjects	Follow-up period	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Covariates	Comments
Schüz *et al.* (2006c) Denmark, 1982–2002	357 553	1982–2002	Records of cellular service providers	Testis (186)	Subscriber	522	1.05 (0.96–1.15)	Age, calendar year of observation	Incidence study; cannot be certain who the user was; phones used under business accounts not included; details of phone use not available
Schüz *et al.* (2006c) Denmark, 1982–2002	420 095	1982–2002	Records of cellular service providers	Salivary gland (142)	Subscriber	26 (males) 0 (females)	0.86 (0.56–1.26) 0.00 (0.00–1.02)	Age, calendar year of observation	Incidence study; cannot be certain who the user was; phones used under business accounts not included; details of phone use not available

d, day; h, hour; SIR, standardized incidence ratio; SMR, standardized mortality ratio; yr, year

lifetime use, nor year of first use. The incidence of NHL was elevated among men who had used cell phones for > 8 years (OR, 2.4; 95% CI, 0.8–7.0, based on 17 cases).

2.3.3 Uveal (ocular) melanoma

In a study of 118 cases and 475 controls, Stang *et al.* (2001) reported an association between assessed occupational use of mobile phones and risk of uveal melanoma (Table 2.19). Methods for this study are described in greater detail in Section 2.1.3. [There was no adjustment for exposure to ultraviolet radiation, which may be a relevant confounder. Exposure information was crude, and concerns were raised about possible bias in the self-reported data in this small study (Johansen *et al.*, 2002).]

The same investigators carried out a much larger case–control study (455 cases; aged 20–74 years) between 2002 and 2004 using a more refined exposure-assessment instrument (Stang *et al.*, 2009; Table 2.19). Three control series were enrolled. One included 827 population controls selected from census data from local districts and matched to case patients on age (5-year age groups), sex and region of residence. A second control series included 180 ophthalmology patients – recruited from practices of the same ophthalmologists who had referred the case patients with uveal melanoma – who had a newly diagnosed benign disease of the eye. The third control group consisted of 187 siblings of cases. Participation rates were 94% for the case patients, 57% for the population and sibling control subjects, and 52% for the ophthalmologists control subjects. The risk of uveal melanoma was not associated with regular use of mobile phones based on any of the three control series (with population controls: OR, 0.7; 95% CI, 0.5–1.0; with ophthalmologist controls: OR, 1.1; 95% CI, 0.6–2.3; and with sibling controls: OR, 1.2 95% CI, 0.5–2.6). There were no associations with cumulative measures of exposure (years of use, number of calls) based on any of the control series. [The Working Group noted the higher participation rate for cases than for controls and the attendant possibility of selection bias.]

The incidence of cancer of the eye (histology not specified, but likely to include a high proportion of melanomas) was not increased in a large cohort of Danish mobile-phone subscribers relative to the general population in a study that reported follow-up until 2002 (Schüz *et al.*, 2006c; Table 2.18).

The substantial increase in use of mobile telephones has not been accompanied by an increase in uveal (ocular) melanoma in the USA up to 2000 (Inskip *et al.*, 2003, 2004), nor was an increase seen in Denmark up to 1996 (Johansen *et al.*, 2002). The annual percentage change in the USA was –0.7% for males (95% CI, –2.3–0.9) and –1.2% for females (95% CI, –2.5–0.0) (Inskip *et al.*, 2003). Narrowing the time window to the 1990s failed to reveal any sign of a recent increase in incidence.

2.3.4 Cancer of the testis

The potential exists for the testes to be exposed to RF radiation if a mobile phone is kept in a trouser pocket while in stand-by mode, or when using a hands-free device. The incidence of cancer of the testis was not increased among 357 533 Danish male mobile-phone subscribers relative to that in the general population, based on an average follow-up of 8 years (maximum, 21 years) (SIR, 1.05; 95% CI, 0.96–1.15) (Schüz *et al.*, 2006c; Table 2.18).

A case–control study of cell-phone use and testicular cancer in Sweden (542 seminomas, 346 non-seminomas, and 870 controls) gave null results for both histopathological subtypes (Hardell *et al.*, 2007b; Table 2.18). Cases were diagnosed between 1993 and 1997.

Table 2.19 Case–control studies of leukaemia, lymphoma and other cancers and use of mobile phones

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Kaufman *et al.* (2009) Thailand, 1997–2003	180	756	Hospital	Interviewer-administered standardized questionnaire	Leukaemia (bone marrow) (204–207)	Ever use Use of GSM services	35 NR	1.5 (1.0–2.4) 2.1 (1.1–4.0)	Matching factors age, sex, area of residence, income, exposure to benzene, solvents, pesticides, or power lines	No association with duration of ownership, lifetime hours of use, or h/yr; short duration of use (median, 24–26 months); also evaluated by subtype of leukaemia
Cooke *et al.* (2010) United Kingdom, 2003–09	806	585	Non-blood relatives	Interviewer-administered standardized questionnaire	Leukaemia (204–207) exclusive of CLL (204.1)	Never, or non-regular use Regular use Lifetime years of use: 0.5–4 5–9 10–14 ≥ 15 *P* for trend	132 674 201 309 110 42 0.30	1.00 1.06 (0.76–1.46) 0.97 (0.67–1.39) 1.10 (0.77–1.58) 1.04 (0.67–1.61) 1.63 (0.81–3.28)	Age, sex, SES, area of residence, ethnicity, smoking, interview lag-time and period	No significant associations with year since first use, lifetime years of use, cumulative number of calls, or cumulative hours of use; low participation rate (50%)
Hardell *et al.* (2005) Sweden, 1999–2002	910	1016	Population	Mail questionnaire + telephone	NHL	*Use of analogue and digital phones (yr)* > 1 > 5 > 10	 130 123 70	 1.02 (0.73–1.44) 1.04 (0.73–1.46) 0.91 (0.61–1.36)	Age, sex, year of diagnosis	Ages 18–74 yr; no differences by subtype of NHL

Table 2.19 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Linet *et al.* (2006) USA, 1998–2000	551	462	Population	Mail + home questionnaire	NHL	Ever use	234	1.0 (0.7–1.3)	Age, ethnicity, education, geographic site	Risk also not significantly associated with min/wk, duration, or year when use started. Results were null for total NHL, large B-cell and follicular lymphoma
						Cumulative use (h):				
						≤ 78	35	0.8 (0.4–1.4)		
						79–208	23	0.8 (0.4–1.5)		
						≥ 209	35	1.1 (0.6–2.1)		
Stang *et al.* (2001) Germany, 1995–98	118	475	Population, hospital	Interview	Uveal melanoma (190)	*Probable/certain mobile-phone use*			Age, sex, geographic area	Crude exposure assessment; low prevalence of exposure; few long-term users
						Ever	6	4.2 (1.2–14.5)		
						≥ 5 yr in past	3	4.9 (0.5–51.0)		
Stang *et al.* (2009) Germany 2002–04	459	1194	Population, ophthalmology, siblings	Questionnaire	Uveal melanoma (190)			*Relative risk*	Age, sex, residence	RR estimates based on population controls; low participation rate among controls (57%)
						Regular use	30	0.7 (0.5–1.0)		
						Cumulative use (yr):				
						≤ 4	17	0.8 (0.5–1.2)		
						5–9	11	0.6 (0.4–1.0)		
						≥ 10	2	0.6 (0.3–1.4)		

Table 2.19 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Hardell *et al.* (2007b) Sweden 1993–97	888 (542 seminoma; 346 non-seminoma)	870	Population	Questionnaire	Testicular cancer (178)	*Cumulative use of mobile-phone (h)*			Age, year of diagnosis, cryptorchidism	Similar null results for seminoma and non-seminoma, as well as by latency
						Analogue:				
						1–127	102	1.3 (0.9–1.8)		
						128–547	46	0.7 (0.5–1.0)		
						> 547	27	0.8 (0.5–1.4)		
						Digital:				
						1–127	85	1.2 (0.8–1.8)		
						128–547	48	0.9 (0.6–1.5)		
						> 547	31	1.1 (0.6–1.9)		
Auvinen *et al.* (2002) Finland, 1996	34	170	Population	Mobile-phone subscriber lists	Salivary gland cancer (142)	Ever (analogue and digital)	4	1.3 (0.4–4.7)	Age, sex	Small number of cases; limited information on exposure; results shown are for analogue and digital phones combined
						Duration (yr):				
						< 1	0	-		
						1–2	3	1.7 (0.4–7.5)		
						> 2	1	2.3 (0.2–25.3)		
Hardell *et al.* (2004) Sweden, 1994–2000	267	1053	Population	Questionnaire	Malignant and benign salivary-gland tumours (142, 210)	Ever use (analogue)	31	0.92 (0.58–1.44)	Age, sex	Only living cases included; latency results are for analogue phones. No cases among long-term users of digital phones
						Ever use (digital)	45	1.01 (0.68–1.50)		
						Latency (yr):				
						> 5	17	0.78 (0.44–1.38)		
						> 10	6	0.71 (0.29–1.74)		

Table 2.19 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Lönn *et al.* (2006) Denmark, Sweden, 2000–02	60	681	Population	Interviewer-administered standardized questionnaire	Malignant parotid gland (ICD codes not reported)	Never regular use of mobile phone	35	1.0	Age, sex, geographic region, education	
						Regular use	25	0.7 (0.4–1.3)		
						Time since start of use (yr)				
						< 5	14	0.7 (0.3–1.3)		
						5–9	8	0.7 (0.3–1.7)		
						≥ 10	2	0.4 (0.1–2.6)		
						Cumulative use (h)				
						< 30	7	0.7 (0.3–1.6)		
						30–449	11	0.7 (0.3–1.4)		
						≥ 450	5	0.6 (0.2–1.8)		
Lönn *et al.* (2006) Sweden, 2000–02	112	321	Population	Interviewer-administered standardized questionnaire	Benign pleomorphic adenomas (ICD codes not reported)	Never regular use of mobile phone	35	1.0	Age, sex, geographic region, education	
						Regular use	77	0.9 (0.5–1.5)		
						Time since start of use (yr)				
						< 5	47	1.0 (0.6–1.8)		Risk for ipsilateral use: OR, 1.4 (95% CI, 0.2–2.2)
						5–9	23	0.8 (0.4–1.5)		
						≥ 10	7	1.4 (0.5–3.9)		
						Cumulative use (h)				
						< 30	20	1.1 (0.6–2.3)		
						30–449	34	0.9 (0.5–1.6)		
						≥ 450	22	1.0 (0.5–2.1)		

Table 2.19 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Sadetzki *et al.* (2008) Israel, 2001–03	460 (48 malignant; 402 benign)	1266	Population	Personal interview	Malignant and benign salivary-gland tumours (142, 210)	Not regular use of mobile phone < 1 yr	175	1.0	Unadjusted (cigarette smoking was considered but did not change OR)	Separate analyses for benign and malignant tumours, with similar results
						Regular use	285	0.87 (0.68–1.13)	Gender, interview date, age, continent of birth	Age at diagnosis, ≥ 18 yr
						Duration of use (yr)				
						1–4.9	138	0.84 (0.63–1.12)		
						5–9.9	134	0.92 (0.67–1.27)		
						≥ 10	13	1.0 (0.48–2.09)		
						Time since start of use (yr)				
						1–4.9	138	0.82 (0.61–1.10)		
						5–9.9	134	0.95 (0.70–1.30)		
						≥ 10	13	0.86 (0.42–1.77)		
						Cumulative use (h)				OR for ipsilateral use: 1.49 (95% CI, 1.05–2.13)
						≤ 266.3	121	0.82 (0.62–1.09)		
						266.4–1034.9	80	1.03 (0.72–1.47)		
						≥ 1 035	83	1.09 (0.75–1.60)		

Table 2.19 (continued)

Reference, study location and period	Total cases	Total controls	Control source (hospital, population)	Exposure assessment	Organ site (ICD code)	Exposure categories	Exposed cases	Odds ratio (95% CI)	Covariates	Comments
Duan *et al.* (2011) China 1993–2010	136	2051	Hospital	Personal or telephone interviews	Salivary-gland cancer (142)	Regular use model	91	1.14 (0.72–1.81)	Age, sex, residential area, marital status, education, income, smoking status	Possible over-parameterization; difficult to reconcile overall RR with exposure category-specific RRs
						No. of calls since first use				
						≤ 24 000	78	1.78 (1.12–2.84)	As above	Implausible RR and CI for highest exposure category (one exposed case)
						24 001–42 000	12	1.76 (1.01–2.51)		
						> 42 000	1	15.36 (13.34–17.38)		
						Duration of use (yr)				
						0–6	67	1.69 (1.05–2.73)	As above	Preceding comments raise serious questions about analysis
						7–8	7	3.69 (2.82–4.57)		
						9–10	2	7.70 (6.20–9.20)		
						> 10	15	4.14 (1.76–9.69)		

CLL, chronic lymphocytic leukaemia; GSM, Global System for Mobile Communications; min, minute; NHL, non-Hodgkin lymphoma; NR, not reported; RR, relative risk; SES, socioeconomic status; h, hour; yr, year

2.3.5 Cancers of the parotid gland

The salivary glands are potentially exposed to high doses of RF radiation from mobile phones, particularly the parotid gland on the side of the head on which the phone is used. Five case–control studies and one cohort study have addressed a possible relationship between cancer of the salivary gland and use of mobile phones.

An early case–control study by Auvinen *et al.* (2002) (Table 2.19) gave null results, but was quite small (34 cases), included only malignant tumours, and provided limited information about details of phone use. Cases were ascertained from the Finnish Cancer Registry and controls from the nationwide population registry. Personal identifiers were linked with subscription records for two cellular networks in 1996. [This register-based approach precludes selection bias to non-response as well as recall bias in the ascertainment of mobile phone use. Information on the frequency or duration of calls was not available, nor was mobile-phone use under a corporate account.]

A case–control study by Hardell *et al.* (2004) (Table 2.19) included 267 cases, considered both benign and malignant tumours of the parotid gland, and provided detailed exposure information. Again, the results were null. [The study included few people who had used mobile phones for > 10 years.]

A case–control study by Lönn *et al.* (2006) (Table 2.19), which was part of the INTERPHONE study, included 172 cases (benign and malignant parotid tumours combined), 681 controls (for the 60 malignant cases), and 321 controls (for the 112 benign cases). The study found no association with regular use of mobile phones for either malignant or benign parotid tumours. The surrogate exposure metrics considered included frequency of use, duration of regular use, time since first regular use, cumulative use and cumulative number of calls. For benign tumours, there was a slightly elevated risk associated with ipsilateral use of mobile phones (OR, 1.4; 95% CI, 0.2–2.2, based on 51 cases) but not for contralateral tumours (OR, 0.7; 95% CI, 0.4–1.1, based on 35 cases). [There may have been bias in reporting of laterality of phone use.]

A case–control study of tumours of the parotid gland was conducted in Israel, where use of mobile phones was reported to be very high (Sadetzki *et al.*, 2008; Table 2.19). This was the largest study of this type (402 cases with benign tumours, 58 with malignant tumours, and 1266 controls), also conducted as part of the INTERPHONE study. Cases were diagnosed at age 18 years or more during 2001 and 2003. In the main analyses, no increased risk was observed for any of the exposure surrogates examined. Laterality analyses generally indicated increased risk for ipsilateral use and reduced risk for contralateral use, e.g. for > 266 hours of cumulative call time with no hands-free devices, the odds ratio for ipsilateral use was 1.49 (95% CI, 1.05–2.13, based on 115 cases), while the odds ratio for contralateral use was 0.84 (95% CI, 0.55–1.28, based on 48 cases). Stratified analyses according to type of residence produced a somewhat higher odds ratio for rural and mixed rural/urban areas than for poor urban areas. For rural and rural/urban users, exposure–response associations were significant for cumulative call time (P = 0.04) and borderline significant for number of calls (P = 0.06). When the analyses were restricted to regular users only, taking the lowest category of use as the reference, increased odds ratios were found if time since start of use was > 5 years before diagnosis (OR, 1.40; 95% CI, 1.03–1.90, based on 134 cases) and for the highest exposure category of cumulative number of calls (OR, 1.51; 95% CI, 1.05–2.17, based on 81 cases) and duration of calls (OR, 1.50; 95% CI, 1.04–2.16, based on 83 cases). [The fact that there were increased odds ratios for ipsilateral tumours and decreased odds ratios for contralateral tumours suggested the presence of bias in reporting side of use.]

In a hospital-based case–control study of epithelial cancers of the parotid gland conducted in China between 1993 and 2010 (136 cases, 2051 controls), no overall association of cancer risk with regular use of mobile phones was observed (Duan *et al.*, 2011; Table 2.19). The authors also evaluated several more detailed exposure metrics and commented that several showed evidence of a dose–response relationship. [This interpretation was made uncertain by aspects of variation in the odds ratios. In several instances, there was no indication of a gradient in risk, but a very large increase in the odds ratio for the highest exposure category. Perhaps more puzzling was the fact that, for many of the exposure variables, odds ratios for all categories of exposure were higher than the overall odds ratio of 1.14. One would expect the overall odds ratio for regular use to be a weighted average of category-specific odds ratios. For number of calls since first use, the authors reported an odds ratio of 15.36 (95% CI, 13.34–17.38) for the highest exposure category, based on one exposed case. This cannot be correct and raises doubt about other analyses. The odds ratio presented may be 1/OR, as 0.7% of cases and 12.6% of controls were in this category.]

The incidence of cancers of the salivary gland was not increased relative to that in the general population in a large cohort of mobile-phone subscribers in Denmark followed up for up to 21 years (Schüz *et al.*, 2006c; Table 2.19).

A recent descriptive study reported an increase in the occurrence of cancer of the parotid gland (not incidence rate) in Israel, which appeared to begin around 1990 and continue through 2006 (Czerninski *et al.*, 2011). [Interpretation of these findings was difficult given the increase in population size in Israel, possible improvements over time in the ascertainment of cancers of the parotid gland, a substantial shift in diagnoses over time from the category "major salivary gland cancers, not otherwise specified" to more precisely defined types – the large majority of which were cancers of the parotid gland – and the lack of information about mobile-phone use.]

2.3.6 Other cancers

(a) Cancer of the breast

[There was little information concerning mobile-phone use and risk of breast cancer.] Breast cancer did not occur more often than expected based on incidence rates in the general population in a cohort of 65 542 Danish female mobile-phone subscribers followed from as early as 1982 until 1995 (Schüz *et al.*, 2006c; Table 2.18).

(b) Cancer of the skin

In a case–control study of cutaneous melanoma in the head and neck region (347 cases, 1184 controls), Hardell *et al.* (2011b) reported no overall association with use of mobile phones (OR, 1.0; 95% CI, 0.7–1.3, based on 223 cases) or cordless phones (OR, 0.9; 95% CI, 0.6–1.2, based on 138 cases), nor among those with heavier use. Use of cordless phones, but not mobile phones, was associated with an increased risk of melanoma in the temporal region, cheek, and ear for the group with 1–5 year latency among those with heavier use (OR, 2.1; 95% CI, 1.1–3.8 for > 365 cumulative hours, based on 21 cases). [The overall pattern in the data pointed more in the direction of no effect. The odds ratio mentioned in the Abstract for the latency period of 1–5 years did not match that in Table 2 of the published manuscript regarding mobile-phone use.]

[To date, there have been no studies of non-melanoma skin cancer in relation to mobile-phone use.]

(c) Other cancer sites

Subscribers to mobile-phone services in Denmark followed from as early as 1982 until 2002 did not show significantly elevated incidence rates of cancers of the lung, larynx, bladder, buccal cavity, oesophagus, liver, uterine cervix, stomach, kidney, pancreas, prostate or other sites, relative to the incidence rates in the Danish general population (Schüz *et al.*, 2006c).

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