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Mobile phone use and brain tumour risk – COSMOS, a prospective cohort study

Maria Feychting [a,*], Joachim Schüz [b], Mireille B. Toledano [c,d,e,f], Roel Vermeulen [g,h], Anssi Auvinen [i,j], Aslak Harbo Poulsen [k], Isabelle Deltour [b], Rachel B. Smith [c,d,e,f], Joel Heller [c], Hans Kromhout [g], Anke Huss [g], Christoffer Johansen [l], Giorgio Tettamanti [a,1], Paul Elliott [c,d,e,m,1,*]

[a] Unit of Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
[b] International Agency for Research on Cancer (IARC/WHO), Environment and Lifestyle Epidemiology Branch, Lyon, France
[c] Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK
[d] Medical Research Council (MRC) Centre for Environment and Health, School of Public Health, Imperial College London, London, UK
[e] National Institute for Health Research (NIHR) Health Protection Research Unit in Chemical and Radiation Threats and Hazards, Imperial College London, London, UK
[f] Mohn Centre for Children's Health and Wellbeing, School of Public Health, Imperial College London, London, UK
[g] Utrecht University, Institute for Risk Assessment Sciences, Utrecht, the Netherlands
[h] University Medical Center Utrecht, Julius Center, the Netherlands
[i] STUK – Radiation and Nuclear Safety Authority, Environmental Surveillance, Vantaa, Finland
[j] Tampere University, Faculty of Social Sciences/Health Sciences, Tampere, Finland
[k] Danish Cancer Institute, Copenhagen, Denmark
[l] CASTLE Cancer Late Effect Research Oncology Clinic, Center for Surgery and Cancer, Rigshospitalet, Copenhagen, Denmark
[m] NIHR Imperial Biomedical Research Centre, Imperial College London, London, UK

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ABSTRACT

Background: Each new generation of mobile phone technology has triggered discussions about potential carcinogenicity from exposure to radiofrequency electromagnetic fields (RF-EMF). Available evidence has been insufficient to conclude about long-term and heavy mobile phone use, limited by differential recall and selection bias, or crude exposure assessment. The Cohort Study on Mobile Phones and Health (COSMOS) was specifically designed to overcome these shortcomings.

Methods: We recruited participants in Denmark, Finland, the Netherlands, Sweden, and the UK 2007–2012. The baseline questionnaire assessed lifetime history of mobile phone use. Participants were followed through population-based cancer registers to identify glioma, meningioma, and acoustic neuroma cases during follow-up. Non-differential exposure misclassification was reduced by adjusting estimates of mobile phone call-time through regression calibration methods based on self-reported data and objective operator-recorded information at baseline. Hazard ratios (HR) and 95% confidence intervals (CI) for glioma, meningioma, and acoustic neuroma in relation to lifetime history of mobile phone use were estimated with Cox regression models with attained age as the underlying time-scale, adjusted for country, sex, educational level, and marital status.

Results: 264,574 participants accrued 1,836,479 person-years. During a median follow-up of 7.12 years, 149 glioma, 89 meningioma, and 29 incident cases of acoustic neuroma were diagnosed. The adjusted HR per 100 regression-calibrated cumulative hours of mobile phone call-time was 1.00 (95 % CI 0.98–1.02) for glioma, 1.01 (95 % CI 0.96–1.06) for meningioma, and 1.02 (95 % CI 0.99–1.06) for acoustic neuroma. For glioma, the HR for ≥ 1908 regression-calibrated cumulative hours (90th percentile cut-point) was 1.07 (95 % CI 0.62–1.86). Over

Abbreviations: CI, Confidence interval; COSMOS, Cohort Study of Mobile Phone Use and Health; CNS, Central Nervous System; DECT, Digital Enhanced Cordless Telecommunications; GSM, 2G, Global System for Mobile Communications; HR, Hazard ratio; RF-EMF, Radiofrequency electromagnetic field; UMTS, 3G, Universal Mobile Telecommunications Service.

* Corresponding authors at: Institute of Environmental Medicine, Box 210, SE-17177 Stockholm, Sweden (Maria Feychting). Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, Norfolk Place, London W2 1PG, UK (Paul Elliott).
E-mail addresses: maria.feychting@ki.se (M. Feychting), p.elliott@imperial.ac.uk (P. Elliott).
[1] Dr Tettamanti and Prof Elliott contributed equally to this article.

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15 years of mobile phone use was not associated with an increased tumour risk; for glioma the HR was 0.97 (95 % CI 0.62–1.52).
Conclusions: Our findings suggest that the cumulative amount of mobile phone use is not associated with the risk of developing glioma, meningioma, or acoustic neuroma.

1. Introduction

Widespread and increasing use of wireless technology has led to concern that health effects such as cancer and other chronic diseases might be associated with prolonged exposure to radiofrequency electromagnetic fields (RF-EMF), even below guideline levels. The energy from RF-EMF is too weak to ionize molecules, and cannot directly damage DNA, but is absorbed by the exposed tissue resulting in heating (Challis, 2005). Radiation protection guidelines protect against excessive heating (Correction of name). If RF-EMF exposure from mobile phones are below levels averaged over time as defined in the guidelines, the exposure would lead to heating within normal physiological variation. As RF-EMF fields decrease rapidly with distance from the source, and exposure is highest during mobile phone calls when the phone is held next to the ear, epidemiologic research on cancer risk due to RF-EMF from mobile phones has mainly focused on intracranial tumours.

Previous epidemiological studies of cancer and mobile phone use have been mostly case-control studies (Roosli et al., 2019); with only two cohort studies (Benson et al., 2013; Johansen et al., 2001; Frei et al., 2011; Schuz et al., 2022). Major limitations of the case-control studies are the retrospective collection of exposure information through interviews or questionnaires, with potential for differential recall between cases and controls (Vrijheid et al., 2009); and selection bias from non-participation (Vrijheid et al., 2009). These biases have not affected the prospective cohort studies, but instead, they have been limited by crude exposure information. In 2011, the International Agency for Research on Cancer (IARC) classified RF-EMF as “possibly carcinogenic to humans”, group 2B (Baan et al., 2011). At the time, only one cohort study was available (Johansen et al., 2001; Schuz et al., 2006; Schuz et al., 2011) and incidence time-trend studies covered only a short period after the broad adoption of handheld mobile phones (Baan et al., 2011). More recent incidence time-trend studies that account for improved surveillance and diagnostics generally indicate no increased incidence correlating with wide-scale adoption of mobile phone use (de Vocht, 2021; Deltour et al., 2022; Elwood et al., 2022; Ostrom et al., 2022; Villeneuve et al., 2021).

The Cohort Study on Mobile Phones and Health (COSMOS) is the largest prospective cohort study of mobile phone use specifically designed to overcome the well-described shortcomings of both case-control and previous cohort studies, through a more comprehensive prospective collection of exposure information, including both self-report and mobile network operator data, while also addressing longer-term exposure and more recent technologies than previous studies (Schuz et al., 2011). Such a study is a high priority research need defined by the World Health Organization (WHO) (Who, 2006; Who, 2010) and the European Commission (SCENIHR, 2009). Here we present the results on mobile phone use and brain tumour risk based on the COSMOS cohort.

2. Methods

2.1. Study population

The COSMOS cohort study recruited participants aged ≥ 18 years from Denmark, Finland, France, Sweden, The Netherlands, and the United Kingdom (UK). French data were not included in the current analysis because baseline data collection in France was conducted late (2017–2019), with too short a follow-up for analysis. Further information about the COSMOS cohort is available elsewhere (Schuz et al., 2011). Recruitment strategies differed between participating countries. To increase statistical power, Denmark, Finland and Sweden invited participants ≥ 18 years of age from mobile network subscriber lists, stratified on age, sex and amount of phone use (Schuz et al., 2011). The UK used a similar strategy for 65 % of their invited participants, while 35 % were invited from the UK edited electoral register (Toledano et al., 2017). The Netherlands recruited participants from three existing cohort studies (AMIGO, EPIC, and Nightingale), two of which mainly included women (Reedijk et al., 2018). A more detailed description of the recruitment and participation can be found in the published cohort descriptions (Schuz et al., 2011; Toledano et al., 2017; Reedijk et al., 2018). All participants answered a baseline questionnaire (postal or web-based) between 2007 and 2012 (Table 1) providing detailed information on current and past mobile phone use. We asked participants for consent to obtain information on their mobile phone use from their operators for a three-month period at baseline, and on health outcomes from national registries and databases.

The study was approved by local data protection boards, research ethics committees or institutional review boards in all countries (Appendix 1).

2.2. Outcome definition

Information on cancer occurrence was obtained through cohort linkage to national cancer registries. In the Nordic countries, linkage was made through the unique personal identity numbers assigned to all residents and used in all national registers, while in the UK linkage to national cancer registries used NHS numbers as the unique identifier. In the Netherlands a range of variables were used to achieve probabilistic linkage of unique individuals. For analyses reported here, we identified incident cases of glioma (ICD10 C71, D33.0-2), meningioma (ICD10 C70.0, D32.0, D42.0), and vestibular schwannoma (ICD10 C72.4, C72.5, D33.3, D43.3), with restriction to appropriate morphology codes (detailed in Supplementary Table S1). Vestibular schwannoma is commonly known as acoustic neuroma, the term used in this paper.

2.3. Exposure variables

At baseline, participants reported the year they started using a mobile phone regularly (≥1 call per week) and their current use: average weekly number and duration of mobile phone calls, and proportion of calls with hands-free device use during the three months preceding baseline. We extracted information from the baseline network operator data on the recorded number and duration of mobile phone calls covering the same period. Participants also reported their past amount of mobile phone and hands-free device use every five years from 1985 onwards to capture changes in use over time. Current and past use was reported categorically (see Appendix C). A 5-year estimate was used to determine exposure for the surrounding 2.5 years according to an *a priori* elaborated analysis plan, see Appendix B. As the time that a mobile phone is held to the ear better reflects RF-EMF exposure to the head, we focused analyses on call duration.

Exposure validation studies have shown both random and systematic measurement errors when healthy volunteers were asked to report their mobile phone use during a recent time-period (Goedhart et al., 2015; Toledano et al., 2018; Vrijheid et al., 2006). To reduce measurement error, we evaluated performance of different statistical methods to adjust estimates of mobile phone call-time by using self-reported data and objective operator-recorded data for the three months preceding the

Table 1
Baseline characteristics of the COSMOS cohort according to the distribution of cumulative hours of mobile phone call-time.

	Total	Cumulative hours of call-time[a]		
	n (%)	<464 hn (%)	464 h – <1062 hn (%)	≥1062 hn (%)
Total	264,574	128,845 (50.0)	64,246 (25.0)	64,383 (25.0)
Person-years	1,836,479	812,245 (45.1)	482,526 (26.8)	504,363 (28.0)
Sex				
Male	94,533 (35.7)	29,854 (32.3)	26,754 (29.0)	35,771 (38.7)
Female	170,041 (64.3)	98,991 (60.0)	37,492 (22.7)	28,612 (17.3)
Age (years)				
18–29	37,548 (14.2)	14,926 (40.7)	12,356 (33.7)	9398 (25.6)
30–39	43,845 (16.6)	16,921 (39.6)	12,666 (29.6)	13,179 (30.8)
40–49	56,468 (21.3)	28,731 (52.2)	12,367 (22.5)	13,972 (25.4)
50–59	69,720 (26.4)	36,072 (53.0)	15,542 (22.9)	16,386 (24.1)
≥60	56,993 (21.5)	32,195 (58.6)	11,315 (20.6)	11,448 (20.8)
Educational level				
Compulsory or less	28,359 (10.7)	14,115 (51.0)	6151 (22.2)	7384 (26.7)
Upper secondary	111,707 (42.2)	62,520 (57.5)	23,173 (21.3)	23,055 (21.2)
University degree or higher	112,694 (42.6)	48,276 (43.7)	31,759 (28.8)	30,413 (27.5)
Missing	11,814 (4.5)	3934 (37.0)	3163 (29.8)	3531 (33.2)
Marital status				
In a relationship	203,350 (76.9)	99,698 (50.2)	49,160 (24.7)	49,918 (25.1)
Single	51,328 (19.4)	25,910 (51.9)	12,550 (25.1)	11,498 (23.0)
Missing	9896 (3.7)	3237 (37.0)	2536 (29.0)	2967 (33.9)
Country (*baseline years*)				
Denmark (*2007–2009*)	25,768 (9.7)	12,122 (48.0)	6753 (26.8)	6369 (25.2)
Finland (*2009–2010/11*)	11,209 (4.2)	812 (7.4)	3229 (29.5)	6914 (63.1)
Sweden (*2007–2009*)	50,163 (18.9)	15,932 (32.5)	12,830 (26.2)	20,203 (41.3)
Netherlands (*2011–2012/13*)	87,689 (31.5)	68,092 (85.0)	10,863 (13.6)	1122 (1,4)
United Kingdom (*2010–2012*)	94,335 (35.7)	31,887 (34.6)	30,571 (33.2)	29,725 (32.2)

[a] Cumulative hours of mobile phone call-time adjusted through regression calibration methods based on operator-recorded information about call duration, with cut-points at the median and 75th percentile. 7100 participants (2.7%) had missing information on cumulative hours of mobile phone call-time.

baseline, the latter available for a subset of participants. In a simulation study with a binary health outcome, we evaluated four regression calibration methods (simple, direct, inverse, and generalized additive model for location, shape, and scale) (Reedijk et al., 2024); in addition to complete-case analysis, and multiple imputation. The simple, direct and inverse regression calibration methods were associated with less bias and lower mean squared error than other methods and provided more accurate estimation of the association between mobile phone use and health outcome (Reedijk et al., 2024). Here we used the simple regression calibration method (the empirical average recorded amount of mobile phone use for each self-reported category). Country-specific regression-calibrated estimates based on operator data for incoming and outgoing mobile phone calls were applied to self-reported weekly mobile phone call-time categories. For the main analyses, the yearly regression-calibrated call-time was summarized into an estimate of cumulative hours of use. For a secondary analysis, we calculated cumulative hours of call-time based on questionnaire exposure category midpoints (denoted "uncalibrated"), for comparability with previous studies that did not calibrate self-reported exposure. Supplementary Figure S1 shows a scatterplot of the regression-calibrated and uncalibrated cumulative hours of use. For both exposure estimates, we used information about baseline and past hands-free device use (hands-free kits in cars, speakerphones, earpieces, video calls, Bluetooth handsets, and the like) to subtract the proportion of call-time with hands-free devices. Use of mobile phones for other purposes, such as texting, was not included in the exposure estimate, as RF-EMF exposure to the head from such use is negligible. If an individual had missing information on the amount of mobile phone use for a specific year, it was imputed using the individual's information from the closest years; however, we excluded participants with imputed values for more than half of the time points from analyses of cumulative hours of mobile phone call-time (n = 2545). In total, 3137 (1.2 %) of the participants included in analyses of cumulative call-time had at least one imputed value.

2.4. Patient and public involvement

Cohort members made important contributions to this research, but they were not involved in the planning, design, or analyses of this study. Cancer patients were identified through Cancer registers, and researchers had no direct contact with the patients.

2.5. Statistical methods

In total, 270,088 participants were linked to national population and cancer registers. Participants who did not provide information about years of regular mobile phone use were excluded (n = 4590, 1.7 %). We excluded 629 participants with any type of central nervous system (CNS) tumour diagnosis before the baseline. Follow-up started six months after baseline to avoid possible influence of prodromal symptoms of an intracranial tumour on memory and mobile phone use; we excluded 295 participants because of death, emigration, or a CNS tumour diagnosis within the first six months after baseline. Supplementary Figure S2 shows a flow-chart of the study population and exclusions. Participants were followed until any CNS tumour diagnosis, emigration, death, or end of follow-up (Denmark: end of November 2016; Finland: end of 2015; Sweden: end of 2017; Netherlands: AMIGO cohort 7th November 2017, EPIC cohort end of 2014, Nightingale cohort 14th June 2017; UK: Scotland end of 2015, England and Wales 1st April 2020).

We calculated the number of years since starting regular mobile phone use from the first year of regular mobile phone use until the year of recruitment into the study and categorized the years as ≤ 9, 10–14, and ≥ 15 years. For acoustic neuroma, we categorized years since first use as < 15 and ≥ 15 years, because of small numbers of cases.

We analysed estimates of cumulative hours of mobile phone call-time until recruitment as continuous variables with effect estimates reported per 100 h call-time, and as categorical variables. They were categorized a priori according to their distribution in the cohort into < median (reference category), 50th – <75th percentile, ≥75th percentile. For glioma, we also conducted an analysis with the 90th percentile as the highest cut-point. Case numbers were too small for corresponding analyses of the other tumour types. A sensitivity analysis was conducted

with categories based on the country-specific distribution of cumulative hours (Supplementary Tables S4-S5).

We estimated hazard ratios (HR) and 95 % confidence intervals (CI) for risk of glioma, meningioma, and acoustic neuroma in relation to mobile phone use through Cox regression models using attained age as the underlying timescale. We used Schoenfeld residuals to test the proportional hazards assumption and found no violations. All regression models were adjusted for country, sex, educational level, and marital status (see Table 1). The original data from Denmark, Finland, the Netherlands, and Sweden were pooled and analysed jointly. As UK data could not be sent outside the UK for legal reasons, they were analysed separately and combined with the results from the other four countries through random-effect meta-analysis. Statistical heterogeneity was evaluated with the Cochran Q-test and the I-squared statistic (Higgins and Thompson, 2002). We defined heterogeneity as a Cochran Q-test with a p-value < 0.05 or an I-squared statistic > 75 %. We managed data using SAS 9.4 and statistical analyses using Stata 16.1.

In a post hoc analysis of glioma, we used ≥ 10 years as the highest cut-point for time since first use, to allow pooling of results with the previous cohort studies (Frei et al., 2011; Schuz et al., 2022; Schuz et al., 2011) in a fixed effects meta-analysis.

3. Results

The final study population included 264,574 participants (Table 1), with a median follow-up of 7.12 years. Overall, 64 % were women, with almost 90 % women in the Dutch cohort and a more even distribution between men and women in the other countries (Supplementary Table S2). Nearly a third (30.5 %) started mobile phone use ≥ 15 years before baseline, and 32.1 % of the observed person-time was in this category, but the proportion varied between countries (Supplementary Table S3). Men had used mobile phones to a greater extent than women (Table 1, Supplementary Table S3). The UK cohort contributed 42.8 % of the person-time (Table 2), Sweden 22.5 %, the Netherlands 21.5 %, while the two other cohorts were smaller. During follow-up, 149 participants were diagnosed with glioma, 89 with meningioma, and 29 with acoustic neuroma (Table 2).

The HR per 100 h regression calibrated cumulative call-time was 1.00 (95 % CI 0.98–1.02) for glioma, 1.01 (95 % CI 0.96–1.06) for meningioma, and 1.02 (95 % CI 0.99–1.06) for acoustic neuroma (Table 3). Results were almost identical for uncalibrated cumulative hours. Results for categorized exposure did not indicate increased risks in higher exposure categories (Table 3). For glioma, the HR for ≥ 1062 h of use was 0.92 (95 % CI 0.58–1.44). The corresponding results for meningioma was 1.08 (95 % CI 0.49–2.35) and for acoustic neuroma 0.86 (95 % CI 0.29–2.53). For glioma, the HR for $\geq$ 1908 regression calibrated cumulative hours (90th percentile cut-point) was 1.07 (95 % CI 0.62–1.86; 20 exposed cases), while the corresponding result for uncalibrated cumulative hours ($\geq$2168 h) was 0.96 (95 % CI 0.54–1.71; 17 exposed cases) (not shown in table). Categorizing exposure according to country-specific distribution of cumulative hours gave similar results, i.e. did not indicate increased risks in higher exposure categories (Supplementary Table S6).

There was no statistically significant heterogeneity between the UK and the other countries for glioma. There was significant heterogeneity between the UK and the other countries in some of the analyses for meningioma and acoustic neuroma. Results from tests of heterogeneity are shown in Supplementary Table S7.

For glioma, the HR for ≥ 15 years since start of regular mobile phone use was 0.97 (95 % CI 0.62–1.52), and for meningioma 1.24 (95 % CI 0.60–2.59) (Table 4). For acoustic neuroma, the HR for ≥ 15 years since first use was 0.76 (95 % CI 0.33–1.73) based on 10 cases, compared to $<$ 15 years (18 cases) (not shown in table). We found no statistically significant heterogeneity between the countries in results for time since start of regular mobile phone use (Supplementary Table S8).

Table 2
Person-years of follow-up and number of incident cases of glioma, meningioma, and acoustic neuroma, according to country, COSMOS cohort.

Country		No. of incident cases		
	Person-years	Glioma	Meningioma	Acoustic neuroma
Denmark	194,193	16	10	2
Finland	51,189	1	3	2
Sweden	413,379	36	25	7
Netherlands	391,652	31	22	6
United Kingdom	786,066	65	29	12
Total	1,836,479	149	89	29

4. Discussion

In this large multinational prospective cohort study, designed specifically to investigate potential health risks associated with mobile phone use, we found no evidence of an association between mobile phone call-time and risk of glioma. Statistical power was limited for meningioma and acoustic neuroma, but the results did not indicate an association. No associations were seen in the heaviest mobile phone users: $\geq$1062 regression-calibrated cumulative hours, about one fourth of all participants, or in the highest decile of cumulative use, $\geq$1908 h ($\geq$2168 uncalibrated hours), the latter analysed only for glioma. Overall, neither regression-calibrated estimates of cumulative hours of mobile phone call-time, nor uncalibrated estimates indicated increased tumour risk at any exposure level. A large proportion of participants had $\geq$ 15 years of regular mobile phone use prior to baseline, and no increased risks emerged among those with the longest history of mobile phone use.

In accordance with our findings, two previous prospective cohort studies, including the earliest mobile phone users, found no association with cancer risk (Frei et al., 2011; Schuz et al., 2022; Schuz et al., 2011). Combining results across COSMOS and these cohorts produced a pooled risk estimate for glioma of 0.94 (95 % CI 0.84–1.04) for ≥ 10 years since first mobile phone use, based on 764 exposed cases (see Supplementary Table S9 for more details). Both previous cohort studies lacked information about cumulative amount of mobile phone use, and neither could assess risks among their heaviest mobile phone users. These limitations were overcome by COSMOS, with detailed exposure assessment for over 250,000 people.

Findings of the largest case-control study to date, Interphone (Interphone Study Group, 2010; Interphone Study Group, 2011); are also broadly consistent with COSMOS, as they showed no increased brain tumour risk in 95 % of the study population, nor an increased risk related to time since starting regular mobile phone use. Interphone, however, reported an increased risk of glioma and acoustic neuroma associated with the highest 5 % of self-reported cumulative call-time, $\geq$1640 h. Interphone assessed the amount of mobile phone use retrospectively through interviews conducted after patients had been diagnosed with a brain tumour, which is prone to recall bias, especially as the tumour and its treatment may affect memory and cognition. Moreover, heavy users in the Interphone study greatly overestimated their mobile phone use; in the $\geq$ 1640 h exposure category the ratio of self-reported to operator-recorded hours was over four (Vrijheid et al., 2009); while such overreporting was not seen in COSMOS (Toledano et al., 2018); despite the more recent use of mobile phones for purposes other than making phone calls. Thus, the $\geq$ 1062 regression calibrated cumulative hours reported by 25 % of COSMOS participants likely represent a considerably higher number of actual accumulated hours than the $\geq$ 1640 h reported in Interphone. An exposure validation study within Interphone found that glioma cases tended to overestimate mobile phone use for more distant time periods (Vrijheid et al., 2009). In addition, in a recent simulation study using the observed exposure measurement error from validation studies of the original Interphone

Table 3
Hazard ratios (HR)[a] and 95% confidence intervals (CI) for the association between cumulative hours of mobile phone call-time and glioma, meningioma, and acoustic neuroma, COSMOS cohort.

	Glioma		Meningioma		Acoustic neuroma	
	No. cases[b]	HR (95 % CI)	No. cases[b]	HR (95 % CI)	No. cases[b]	HR (95 % CI)
Regression calibrated cumulative hours[c]						
<464	66	1 (ref)	48	1 (ref)	12	1 (ref)
464–1061	36	0.99 (0.64–1.52)	13	0.57 (0.27–1.22)	8	0.97 (0.05–17.54)[e]
≥1062	38	0.92 (0.58–1.44)	24	1.08 (0.49–2.35)	8	0.86 (0.29–2.53)
Linear effect per 100 h		*1.00 (0.98–1.02)*		*1.01 (0.96–1.06)*[e]		*1.02 (0.99–1.06)*
Uncalibrated cumulative hours[d]						
<301	72	1 (ref)	51	1 (ref)	12	1 (ref)
301–962	37	0.98 (0.64–1.51)	11	0.51 (0.26–0.99)	8	1.30 (0.27–6.42)
≥963	31	0.77 (0.49–1.22)	23	1.14 (0.47–2.76)	8	1.09 (0.39–3.05)
Linear effect per 100 h		*1.00 (0.98–1.02)*		*1.01 (0.98–1.04)*		*1.02 (0.99–1.05)*

[a] Adjusted for country, sex, education, marital status, with attained age as underlying timescale.
[b] Number of cases do not add up because of missing data on covariates and/or cumulative call-time.
[c] Cumulative hours of mobile phone call-time adjusted through regression calibration methods based on operator-recorded information about call duration, with cut-points at the median and 75th percentile. 7100 participants (2.7%) had missing information on cumulative hours of mobile phone call-time.
[d] Uncalibrated cumulative hours of mobile phone call-time calculated from the midpoint of the response categories, with cut points at the median and 75th percentile.
[e] p for heterogeneity < 0.05.

Table 4
Hazard ratios (HR)[a] and 95% confidence intervals (CI) for the association between time since start of regular mobile phone use and glioma and meningioma, COSMOS cohort.

	Glioma		Meningioma	
	No. cases[b]	HR (95 % CI)	No. cases[b]	HR (95 % CI)
Years of use				
0–9	47	1 (ref)	31	1 (ref)
10–14	39	0.81 (0.51–1.28)	27	1.22 (0.32–4.69)
≥15	58	0.97 (0.62–1.52)	29	1.24 (0.60–2.59)

[a] Adjusted for country, sex, education, marital status, with attained age as underlying timescale.
[b] Number of cases do not add up because of missing data on covariates and/or cumulative call-time.

questionnaire under the assumption of no association between mobile phone use and glioma risk, it was found that a larger variance in reporting errors among cases than among controls contributed to a J-shaped exposure–response relationship, as the one observed in Interphone (Bouaoun et al., 2024). These results and the inconsistency with COSMOS results strengthens the implication that the modest risk increase in the 5 % heaviest mobile phone users in Interphone may have been due to reporting bias.

Furthermore, COSMOS results align with incidence time-trend studies from countries with well-established cancer registries. These found no increase in the incidence of brain tumours in age groups that have been the most frequent mobile phone users (de Vocht, 2021; Deltour et al., 2022; Elwood et al., 2022; Ostrom et al., 2022; Villeneuve et al., 2021); with the advantage of adding more than 10 years of follow-up to the incidence time-trend studies available at the time of the IARC evaluation in 2011 (Baan et al., 2011).

In contrast to COSMOS and all other studies including incidence time-trend studies, also from the Nordic countires (Deltour et al., 2022); a case-control study series in Sweden reported substantially increased risk estimates for glioma and acoustic neuroma associated with mobile phone use, even after very few cumulative hours of use and a short time after starting mobile phone use (Hardell et al., 2006; Hardell et al., 2013; Hardell et al., 2005). Recall bias may be a potential explanation for these findings, as well as other methodological issues (Ahlbom et al., 2009).

For meningioma, almost all case-control studies have reported no association between mobile phone use and tumour risk (Roosli et al., 2019).

A key strength of our study is the large multinational cohort with prospectively collected detailed information about time since start of regular mobile phone use, amount of use, and handsfree device use, through standardised questionnaires that captured changes in use over time. This allowed us to collect information about past mobile phone use unaffected by the disease outcomes, thereby avoiding recall bias. In addition, we obtained objectively recorded operator data on mobile phone call duration for the same time period, allowing us to reduce potential non-differential exposure measurement error and exposure misclassification through regression calibration methods (Reedijk et al., 2024). Nevertheless, some degree of non-differential exposure misclassification is inevitable in self-reported retrospective information in both cohort and case-control studies. Such misclassification will not affect risk estimates in the absence of a real association, but may dilute an association if an effect truly exists. We did not estimate exposure after baseline, but considering that this refers to very recent exposure which is unlikely to be relevant for the development of solid tumours, the potential non-differential exposure misclassification introduced is unlikely to materially affect the risk estimates. Absorbed energy in the brain from RF-EMF exposure during mobile phone calls is also affected by the quality of the connection between the mobile phone and the base station, as the better the quality the lower the output power (and emissions) of the mobile phone, whereas output power is kept at maximum when the connection is of poor quality. This source of exposure variation affects both cohort and case-control studies and is difficult to measure in large-scale epidemiological studies.

There are few established risk factors for brain tumours. We adjusted for age and sex and in addition some sociodemographic variables that may affect timing of the brain tumour diagnosis and are potentially related to mobile phone use. The only established exogenous risk factor, ionizing radiation is unlikely to be related to mobile phone use. Our main limitation is the somewhat limited statistical power, especially for acoustic neuroma, and to some degree for meningioma, resulting in larger uncertainty in results for these tumours, and prevented detailed stratified analyses. Statistically significant heterogeneity between the UK and the other countries was found in some analyses of meningioma and acoustic neuroma, which may reflect differences in ascertainment for these mostly benign tumours across countries.

Authoritative expert committees that relatively recently comprehensively reviewed the scientific evidence concluded that the available evidence does not support an increased risk of brain tumours from low-level RF-EMF exposure emitted during mobile phone calls (SCENIHR, 2015; FDA, 2020); but the evidence was insufficient to conclude about long-term and heavy mobile phone use. COSMOS was specifically designed to address these knowledge gaps (Schuz et al., 2011); by including a large proportion of long-term heavy mobile phone users to increase statistical power.

Today's mobile phone use and low-level RF-EMF exposure from other sources differ substantially from the past exposures experienced by COSMOS cohort participants. Generally, RF-EMF exposure levels to the head during calls have decreased considerably with each new generation of mobile phone technology, most notably between the 2nd (e.g., GSM introduced in the early 1990s) and 3rd generation (e.g., UMTS introduced in the early 2000s); the contribution to the whole-brain RF-EMF exposure from a mobile phone held to the ear while calling on a GSM phone is orders of magnitude higher than that from a 3G phone or a DECT phone (van Wel et al., 2021). At the time of our recruitment, GSM technology was still commonly used, and all long-term mobile phone use prior to the baseline would have been on GSM phones or first-generation analogue phones, and therefore the dominant exposure sources of relevance for assessment of potential long-term effects. Future updates of the COSMOS cohort on cancer outcomes will provide additional information on potential long-term effects of RF-EMF from more recent technology.

In conclusion, in the first follow-up of COSMOS, the world's largest multinational prospective cohort study specifically designed to investigate potential health risks of mobile phone use, we found no evidence that long-term or heavy mobile phone use is associated with the risk of glioma, meningioma, or acoustic neuroma, although results for meningioma and acoustic neuroma are based on small numbers of cases. Our findings to date, together with other available scientific evidence, suggest that mobile phone use is not associated with increased risk of developing these tumours.

CRediT authorship contribution statement

Maria Feychting: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Joachim Schüz:** Writing – review & editing, Methodology, Conceptualization. **Mireille B. Toledano:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Roel Vermeulen:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Anssi Auvinen:** Writing – review & editing, Methodology, Investigation, Funding acquisition, Conceptualization. **Aslak Harbo Poulsen:** Writing – review & editing, Methodology, Investigation. **Isabelle Deltour:** Writing – review & editing, Methodology, Conceptualization. **Rachel B. Smith:** Writing – review & editing, Project administration, Methodology, Investigation. **Joel Heller:** Writing – review & editing, Project administration, Formal analysis. **Hans Kromhout:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Anke Huss:** Writing – review & editing, Project administration, Methodology. **Christoffer Johansen:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Giorgio Tettamanti:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Paul Elliott:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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Expert committee work: M.F. has served as advisor to a number of national and international public advisory and research steering groups concerning the potential health effects of exposure to non-ionizing radiation, including the WHO (ongoing), Public Health England Advisory Group on Non-ionising Radiation - AGNIR (2009-17) , the Norwegian Public Health Institute (2010-12), the Swedish Council for Working Life and Social Research (2003-2012), Swedish Radiation Safety Authority's independent scientific expert group on electromagnetic fields (2003-11). She was member of the International Commission on Non-Ionizing Radiation Protection (ICNIRP), an independent body setting guidelines for non-ionizing radiation protection (2008-May 2020), and vice chairman of the Commission May 2016-May 2020. A.H.P. Is a member of the Swedish Radiation Safety Authority's independent scientific expert group on electromagnetic fields since 2018. A.A. has been a member in expert panels on health effects of radiofrequency electromagnetic fields for International Commission on Non-Ionizing Radiation Protection (ICNIRP), Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) of the European Commission, Swedish Radiation Safety Authority (SSM), and World Health Organization (WHO). AH is a member of the Swedish Radiation Safety Authority's independent scientific expert group on electromagnetic fields since 2012, and since 2021 serves as chair of the group. She is a member of ICNIRP since 2020; and a board member of the BioEM society (2021-2023). She was member of the EMF committee of the Health Council of the Netherlands from 2015-2022. From 2014-2023, she was a member of the scientific council of the Swiss Research Foundation for Electricity and Mobile Communication (FSM), a non-profit foundation. H.K. was the chair of the EMF committee of the Health Council of the Netherlands from 2017-2022. He is currently a member of the WHO Task Group on Radiofrequency Fields and Health Risks. M.B.T is a member of the expert UK Committee on Medical Aspects of Radiation in the Environment (COMARE).

Appendixes A-C. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2024.108552.

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