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Original article

Investigation of bias related to differences between case and control interview dates in five INTERPHONE countries

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ABSTRACT

Purpose: Associations between cellular telephone use and glioma risk have been examined in several epidemiological studies including the 13-country INTERPHONE study. Although results showed no positive association between cellular telephone use and glioma risk overall, no increased risk for long-term users, and no exposure-response relationship, there was an elevated risk for those in the highest decile of cumulative call time. However, results may be biased as data were collected during a period of rapidly increasing cellular telephone use, and as controls were usually interviewed later in time than cases.

Methods: Further analyses were conducted in a subset of five INTERPHONE study countries (Australia, Canada, France, Israel, New Zealand) using a post hoc matching strategy to optimize proximity of case-to-control interview dates and age.

Results: Although results were generally similar to the original INTERPHONE study, there was some attenuation of the reduced odds ratios and stronger positive associations among long-term users and those in the highest categories for cumulative call time and number of calls (eighth–ninth and 10th decile).

Conclusions: Proximity and symmetry in timing of case-to-control interviews should be optimized when exposure patterns are changing rapidly with time.

Introduction

Associations between radiofrequency (RF) electromagnetic field exposure from cellular telephones and brain tumor risk have been examined in a number of epidemiological studies including INTERPHONE [1–10]. INTERPHONE is the largest case-control study

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of the association including over 2700 glioma cases from 13 countries [10]. The odds ratio (OR) for glioma related to any regular use (in the past ≥1 year) of cellular telephones was 0.81 (95% confidence interval [CI], 0.70–0.94): it was 0.98 (95% CI, 0.76–1.26) for 10+ years since start of use [9]. There was an elevated risk among those in the 10th decile of cumulative call time (OR 1640+ hours vs. never regular user = 1.40, 95% CI, 1.03–1.89), although there were some implausible values of use. ORs across the first nine deciles were generally <1.

Possible sources of bias in INTERPHONE including selective nonparticipation and recall bias have been investigated. In an analysis of nonresponse questionnaires (people who did not participate were asked to answer a brief questionnaire), nonparticipation was associated with a lower prevalence and more recent start of cellular telephone use [11]. This was estimated to bias ORs downward by approximately 10% for all users. Comparison of self-reported use to estimates based on network operator records within the previous 4–5 years demonstrated underestimation of number of calls and overestimation of call duration among both cases and controls, the extent of which increased among cases (but not controls) with increasingly early use, possibly resulting in a positive bias in ORs in the moderate past [12]. Participation rates in INTERPHONE were also low.

The fact that, on average, controls were interviewed later in time than cases is another potential source of bias [10,11]. This delay could cause controls to report apparently greater cellular telephone use than cases as usage was rapidly increasing during the period of participant recruitment [13]. A lag between control and case interviews is also more likely to occur with highly fatal and fast-moving diseases such as glioma, which prioritize rapid case ascertainment. Cellular telephone use at the time of interview may also influence recall of previous use, and if usage is generally increasing in time, subjects with later interviews may overestimate past usage compared with subjects with earlier interviews.

Sensitivity analysis in INTERPHONE restricted to case:control pairs in which controls were interviewed within 1 month of the case interview showed little change in the OR for the 10th decile of cumulative call time [9]. However, this analysis was based on only 46 exposed cases and did not consider the full distribution of differences in case-to-control interview dates or range of cellular telephone use metrics. Further work on time-related case-to-control matching in epidemiological studies of cellular telephone use is needed, including better understanding the impact of matching algorithm and analytic strategy on associations observed.

This article investigated an alternative post hoc matching process to optimize proximity of case-to-control interview dates and age in a subset of five INTERPHONE study countries (Australia, Canada, France, Israel, New Zealand) and its impact on associations between cellular telephone use and glioma risk. This five country data set has previously been used to examine associations between RF energy absorbed at the tumor location and brain tumor risk [14]. Some results were reported in an abstract [15].

Materials and methods

Study population

INTERPHONE is a population-based case-control study of primary glioma cases (as well as cases of meningioma, acoustic neuroma, and parotid gland tumors) aged from 30–59 years conducted between 2000 and 2004 [9,10]. Every attempt was made to recruit cases, particularly glioma cases, as rapidly as possible with a median lag-time between case diagnosis and interview ranging from 2 months in France to 8 months in Canada (Ottawa) in the five country data set. Completeness of case recruitment was assessed using secondary sources, and all cases were confirmed histologically or by unequivocal diagnostic imaging. The anatomic location of the tumor was ascertained from medical records. A total of 1302 eligible glioma cases were identified, and 829 were interviewed (64%).

One control was randomly selected for each glioma case (as well as one control for each case of meningioma, two for acoustic neuroma, and three for parotid gland tumors) from the source population in each study center using locally appropriate sampling frames (i.e., electoral lists, health/population registries, or random digit dialing). Controls were matched to cases by age (5-year groups), sex, country-region, and country of birth (Israel only); they were individually matched in Canada (Ottawa, Vancouver), France, Israel, and New Zealand. They were frequency matched in Australia and Canada (Montreal) where they were then matched post hoc to cases by age (5-year groups), sex, and country-region with a single control selected based on the shortest time interval between case diagnosis and control interview and subsequently case and control interview to define the reference date and laterality and location of tumor. The reference date for controls was the date of case diagnosis in each matched set. The response rate among all controls in the five country data set was 53%. Proxy respondents were used for 120 (14%) glioma cases and 14 (0.05%) controls.

Written informed consent was given before the study interview. All appropriate national and local research ethics boards approved the study, including the Ethical Review Board of IARC (Lyon) for INTERPHONE, and the Municipal Institute for Medical Investigation Barcelona for data from the five countries that agreed to transfer their data there.

Data collection

Detailed data on cellular telephone use were collected by trained interviewers as part of a computer-assisted personal interview. For regular cellular telephone users (at least one call per week for 6+ months), data were collected on the phone, network operator, number of calls, duration of calls, and patterns of use. Data were also collected on the use of hands-free sets, the side of the head on which the phone was usually used, and whether the participant was left or right handed, as well as other personal and demographic data.

Exposure assessment

Indicators of regular use, time since start of use (years), cumulative call time with no hands-free devices (hours), and cumulative number of calls with no hands-free devices (in hundreds) were calculated according to the cutpoints of the original INTERPHONE analysis then collapsed here due to the smaller sample size of the five country data set [9]. All indicators were calculated with a 1-year lag, with the exception of time since start of use, where the year before the reference date was treated as never regular use and included in the reference category.

Statistical analysis

This analysis is based on an alternative post hoc matching strategy developed with the aim of minimizing the potential for bias due to differences in case-to-control interview dates and age. The matching algorithm was used to conduct post hoc individual matching in all five study countries, including those where individual matching was originally performed, using the pool of all available controls, including those originally selected for other tumor sites. Controls were restricted to those interviewed within 1