

Scientific report

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Period: from 12/10/2009 to 17/10/2009 Place: 4051 Basel (CH)

Purpose of the visit

The purpose of the STSM was to plan the data analyses for the CEFALO study, an international case-control study of childhood brain tumors. The main goal of the study is to investigate whether use of mobile phones increases the risk of developing brain tumors in children and adolescents in the age group 7-19 years. The planning of the data analysis included statistical modeling regarding use of mobile phones, discussion of statistical methods, and the possibility of developing new methods for quantifying mobile phone use. It also involved planning a strategy for dealing with differences in data from mobile phone operators in the different countries.

Description of the work carried out during the visit

1. Description of CEFALO study
2. Basic analysis strategy across countries
3. Data cleaning and management
4. Statistical modeling and use of potential confounding variables
5. Description of the main results obtained

1. Description of CEFALO study

The CEFALO study is a nationwide case-control study performed in Denmark, Norway, Switzerland and Sweden. The study period was from January 2004 (Denmark), April (Sweden) or May (Norway and Switzerland) until April 2008 (Norway and Switzerland), June 2008 (Denmark), and August 2008 (Sweden).

Cases

Cases were all children diagnosed during the study period with intracranial central nervous system tumors (CNS) in the age 7 to 19 years at the time of diagnosis. The choice of age-range expected to increase the probability of exposure to mobile phone use. All diagnoses were either histologically confirmed or based on unequivocal diagnostic imaging. Medical records were examined to confirm diagnosis and to establish date of diagnosis, which was used as reference date in the exposure assessment. The date of diagnosis was defined as the date when the first x-ray was taken. The completeness of case ascertainment was verified through search in appropriate population-based cancer registries.

Controls

For each case two controls were randomly selected from a population register of the total population of the study area, matched on age (year and month of birth), gender, and residential area. The reference date for controls was the date of diagnosis of cases. Controls diagnosed with Mb Recklinghausen and tuberose sclerosis were excluded. Other exclusion criteria's were deafness, severe mental retardation and poor language skills.

Data collection

All cases and controls were initially informed about the study and asked to participate. For cases, the treating physician gave authorization for invitation, before contact was initiated.

This was done in agreement with local Ethics Review Boards in each country.

Whenever possible, the child and at least one of the parents were interviewed face-to-face by trained interviewers using a computer-assisted personal interview (CAPI) questionnaire (Denmark and Norway) or a paper version of the questionnaire (Switzerland and Sweden). In exceptional cases, telephone interviews were conducted with difficult-to-reach subjects or an adjusted paper version of the questionnaire was sent to the study participant.

The translations of the questionnaire were validated and the questionnaires were pilot-tested in all participating countries.

Mobile phone exposure assessment

All study participants were asked if they had ever spoken on/used a mobile phone more than 20 times during their lives, and if they had ever owned a mobile phone. Owners of a mobile phone were also asked how many different mobile phone subscriptions they have had, the date when they first started using their first mobile phone, make and model of the phone, operator, when they stopped using the phone, how many incoming and outgoing calls per day, week or month with each subscription, and the duration of these calls. If changes in use of mobile phone occurred within a subscription, then this was registered by subdividing the subscription into periods. To ensure the most accurate measure of the actual use of mobile phone by the child, questions about lent out of own mobile phone as well as the child's use of other mobile phones were asked. Furthermore, mobile phone users were asked on which side of the head they generally held the mobile phone, and about use of hands free equipment. In addition, data from mobile phone operators were available.

2. Basic analysis strategy across countries

The analysis of this study will be based on conditional logistic regression. During the meeting a comprehensive discussion of the mobile phone variables were made.

For validation of the data on mobile phone use based on the questionnaires, we discussed the various possibilities of using operator data from three of the four participating countries. For Sweden and Denmark it was possible to validate the questionnaire based mobile phone data. Operators were able to provide information of the recorded use of mobile phone for the period stated in the questionnaire. For Switzerland operators are only allowed to save information about connections on mobile phone use for six months. Thus, billing and subscription duration data is available for lifetime exposure, but it is not possible to have connection data from the actual time period, where the mobile phone was used prior to diagnosis date. Based on the information available from the Swiss operators, a validation of the controls could be possible. In this study we presume that the pattern of mobile phone use for controls have not changed dramatically over time. If any change, we could assume a slight increased use, which should be taken into account when interpreting the validation of the results of the validation.

3. Data cleaning and management

During the STSM meeting, large effort was put on data cleaning and data management. It is essential to obtain a consistent dataset across country. A protocol for the data cleaning process and data management has been developed.

4. Statistical modeling and use of potential confounding variables

Based on the discussion during the STSM meeting, further analysis will contain some core confounding variables. These should always be included in further analysis.

Simulation study

The main purpose of simulation is to assess the impact of recall and participation bias in a case-control study. First, a large source population containing 200000 subjects will be generated. Then, each subject will be assigned either a user or a non-user of mobile phones. Next, all users will be assigned a true exposure (cumulative number of calls) by sampling from a lognormal distribution with known parameters. A logistic function will then be used to assign a probability of disease for each subject. To simulate recall bias, the assigned exposure is multiplied by a log-normally distributed factor to obtain the observed exposure. The parameters of this factor will be allowed to vary according to defined scenarios. A random sample containing 350 cases and 655 controls will be drawn from the source population. Then, the odds ratio is calculated using a logistic regression. The observed exposure is used as independent variable. To simulate the participation bias, the probability of participating in the study varies among users and non-users of mobile phones.

The results of these simulations will play an important role in interpreting the future results from the CEFALO study.

To validate the questionnaire-based mobile phone data, we will compare self-reported and operator-recorded number of calls per month and average duration of calls per month for the Danish and Swedish study participants.

In addition, we plan to compare self-reported data on the start of subscription with the corresponding information from the operator. These data are available in Denmark, Sweden and Switzerland.

5. Description of the main results obtained

We expect this project to provide well documented information about the relationship between reported use of mobile phone and the actual use obtained from mobile phone operators. Information about mobile phone use is often based on self-reported use and information from mobile phone companies is rarely available. This study provides a unique chance of validating questionnaire based mobile phone use at individual level. We expect this validation to be beneficial for future studies of questionnaire-based mobile phone use. In addition we will also provide novel information on how to interpret self-reported mobile phone use.

The visit was extremely useful for managing and cleaning the dataset. We were able to move a substantial step forward in putting together the data from each country in one international data set. We found time to discuss and resolve inconsistencies in the data between countries. After this STSM it is expected that the international dataset can be finalized a few weeks after the visit.

We were able to create some preliminary results for validation of self-reported mobile phone use. We also identified confounding variables in relation to childhood brain tumors and use of mobile phones. These confounders were discussed and categorized for future use in analyses of the CEFALO data.

In measuring mobile phone data we discussed and tested the use of simulation and validation. This way of measuring mobile phone use will give information on trends that can be useful for future studies.

Finally, it was beneficial to address the differences in mobile phone operator data from Denmark, Switzerland and Sweden in order to ensure high quality data for further analysis. This will also provide knowledge on data collection from mobile phone operators in future studies.

Projected publications/articles resulting or to result from the STSM

The STSM meeting will result in an article on validation of questionnaire-based mobile phone data as well as an article regarding assessment of the impact of recall and participation bias in a case-control study.

Confirmation by the host institute of the successful execution of the mission

The STSM was very intensive and successful. Many issues related to the data could be directly clarified, which would have been less effective and accurate if done by e-mail or phone. The international pooled dataset could be almost finished. We could discuss future analyses strategies in detail. Thus, I am convinced that this STSM contributes a successful conduct of the CEFALO study.

Basel, 12 November, 2009, Prof. PhD Martin Röösli

