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International Agency for Research on Cancer (IARC/WHO)
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Presenting: **Mobilphone use and Gliom-Inzidenz since 1979**

Will be published soon – the report is in finalization phase – as soon as possible…

As it was announced at the BfS 2019 (Text translatet with deepl)
http://doris.bfs.de/jspui/bitstream/urn:nbn:de:0221-2020100623424/3/BfS_2020_SCHR_66-20.pdf

Thema Nutzung von Mobiltelefonen und Verlauf der Gliom-Inzidenz seit 1979 **Subject** *The use of mobile phones and the development of glioma incidence since 1979*			
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1. OBJECTIVES.

Radiofrequency electromagnetic fields were classified as "possibly carcinogenic to humans" by the International Agency for Research on Cancer (IARC) in 2011. The study situation on this topic remains inconclusive.

The assessment at that time was based in particular on the results of the Interphone study, an international case-control study published in 2010 on brain tumor risk in relation to cell phone use. The study found a slightly increased brain tumor risk in the highest use category. Moreover, this finding was more pronounced among so-called "unilateral" users, those who held the cell phone on the same side of their tumor location when using the phone (INTERPHONE, 2010). Furthermore, strongly elevated risk estimates were found in a number of Swedish case-control studies using a similar question.

Since the 2011 IARC assessment, the French CERENAT case-control study found an increased risk of meningioma in the highest use group. In turn, this association could not be confirmed in two much larger cohort studies, the UK Million Women Study and a Danish study on this topic. However, all the studies listed have methodological weaknesses (e.g., retrospective and subjective recording of own cell phone use).

Most recently, two recently published long-term exposure studies in rats found increased cardiac schwannomas as well as malignant brain tumors in rats in the respective highest use category. However, the results of the studies were inconsistent across different exposure conditions and the levels of RF-EMF exposure were unrealistic for normal use conditions in humans.

An actual deleterious effect of cell phone use that would lead to an increase in brain tumor risk should equally lead to a detectable increase in the incidence rate in the population because of the frequent use of this technology in the population. However, following this hypothesis, an analysis by Deltour et al. published in 2012 based on cancer registry data from the Nordic countries failed to find an association between cell phone use and incidence curves of brain tumors for the period from 1979 to 2008.

2. INDIVIDUAL OBJECTIVES

The still inconclusive study situation and the high public health relevance due to the widespread use of mobile phones make a re-evaluation of brain tumor incidence rates urgently necessary. Following the statistical approach of Deltour et al., the incidence rates in the Nordic countries Denmark, Sweden, Norway and Finland from 1979 to the present time will now be re-evaluated, especially with regard to

possible change points in the temporal trends.In a simulation study, different risk estimators observed in case-control and cohort studies will be tested for their plausibility. Here, with regard to brain tumors (gliomas), possible scenarios not considered in previous analyses are simulated, for example, latency periods of more than 15 years and lower risk estimators than found in the literature. In addition, different glioma types are examined in a laterality-specific manner.

3. METHODOLOGY

3.1 OBTAINING THE REQUIRED DATA

Brain tumor incidence rates for different types of gliomas and tumor locations for the period from 1979 to the present are extracted from cancer registries in Denmark, Finland, Norway, and Sweden, as far as possible. Relevant demographic data (e.g., sex, age) are provided by the national population registries.

Trends in population exposure, in terms of changes in typical usage behavior, are extrapolated to the total population from objective cell phone usage data from the COSMOS1) study.

COSMOS is a pan-European prospective cohort (with IARC participation) on this topic that uses official network operator usage data for exposure assessment, thus providing an objective measure of actual usage. COSMOS is conducted in Denmark, Finland, and Sweden, among other countries, which also provide data on incidence rates.

To calculate exposure, first the average exposure per use category (high, medium, low) is calculated from the COSMOS data and the population sizes of the user categories (including non-users) are determined. Last, the objective average values per user category are converted to the population sizes in the total population.

3.2 STATISTICAL EVALUATION

Step 1: Calculation of age-standardized incidence rates for each calendar year, including analysis of temporal trends and localization of possible change points (i.e., time points at which the trend in incidence rates changes significantly with respect to previous years), for gliomas overall and for the most common subtypes.

Step 2: Predict the number of glioma cases expected annually assuming different risk scenarios in simulation studies. The risk scenarios are based on the assumption of different risk estimators (percent increase in incidence) for different exposure categories measured by call time. The risk estimators are primarily based on values determined in relevant studies (e.g., Interphone, Hardell studies, cohort studies). In addition, scenarios with more conservative risk estimators are also evaluated. Here, the exposure distribution (distribution of average call duration in the population) is extrapolated to the total population using the objective cell phone usage data from the COSMOS study.

Step 3: The incidence trends thus obtained from the simulation study are compared with the true incidence rates observed in the national population to evaluate the plausibility of the observed risk estimates. This plausibility is indicated by a likelihood, which indicates how likely it is to obtain the observed incidence trend assuming the particular risk model. A high probability indicates compatibility between the risk estimators and the incidence trend; a probability close to 0% would indicate that the risk estimators obtained in the studies are not compatible with the observed rates.

4. IMPLEMENTATION

After obtaining the necessary permissions for data access in the first work package (WP 1), the data set for the analyses was built and prepared in WP 2. The implementation of the EU General Data Protection Regulation was much more complex than planned and caused significant delays in the project, as cancer registries were not allowed to provide incidence data in the previously agreed format. IARC had to develop a data management syntax that would present the incidence data in aggregated, tabular form and thus also allow data transfer in tabular form rather than in individual data. AP 2 could therefore be completed late.

Denmark's brain tumor incidence data were provided to IARC in tabular form for the period 1990-2016. From Finland, anonymized individual data for all intended endpoints for the period 1990-2006 and for the

period 2006-2017 were submitted to IARC. The corresponding Swedish individual data have been available to IARC since September 2019. The Norwegian incidence data were provided to IARC on in tabular form. The extensive plausibility checks of the data with corresponding queries and checks of the original data have now been completed. With the data from the previous project, incidence data for the period 1979-2016 are thus available. The data have been merged into a common dataset. The COSMOS data are held in each of the COSMOS participating countries Finland, Sweden, and Denmark (Norway was not part of the COSMOS study).

5. RESULTS

The project should have been completed on 31/12/2019 as scheduled. However, as the implementation of the EU General Data Protection Regulation has caused significant delays, no results are yet available.

6. PLANNED FURTHER WORK

The evaluation of the data according to the methods described in 3.2 will be carried out by the IARC in the lead of Dr. Isabelle Deltour

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