Cosmos Short Report

The increasing use of mobile phones during the last years and the lack of valid scientific knowledge in this field up-to-now requires further research in this field urgently, especially on long term effects and frequent use.

Due to the widespread use of mobile phones and the up-to-now lack of valid scientific knowledge on possible adverse health effects on their use, especially on long term effects and frequent use, further research in this field is urgently needed.

The Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI) of the University of Mainz was commissioned by the Federal Agency for Radiation Protection (Bundesamt für Strahlenschutz, BfS) to perform a feasibility study for a prospective cohort study of mobile phone users. The term for this feasibility study was limited to 10 months and ended on 31 May 2005.

Aim of this feasibility study was to evaluate if it is possible to perform a prospective cohort study on mobile phone use in the Federal Republic of Germany within an international co-operation.

A prospective cohort study is designed in a way that data on exposure (here: use of mobile phones) will be collected from the beginning of the study. In the course of the follow-up data on diseases and their symptoms, as well as other data like life style factors will be collected continuously. It is important that these data can be collected as a time line of exposure and the diseases under investigation.

Scientific Knowledge

Up to now all in-vitro studies and in-vivo studies with exposure to radio frequency electro-magnetic fields (RF-EMF) were not able to show a clear picture to adverse health effects. A damage of tissue or organs by RF-EMF below legal limits has not been proven yet (see: Assessment of the Radiation Protection Commission (Strahlenschutzkommission SSK on http://www.ssk.de). Nevertheless, there are a several open questions which request more research. A detailed overview of the actual status of the research can be found in reviews of the contractor (Berg et al., 2003; Schüz, 2004).

Up-to-now most epidemiological studies concentrated their research on tumors of head and neck and mobile phone use (Auvinen et al., 2002; Hardell et al., 1999, 2002, 2003; Inskip et al., 2001; Muscat et al., 2000, 2002). The knowledge gained from these studies has to be regarded as not sufficient, especially, as nothing can be stated on a possible decreased risk regarding selected topographies of the tumors or of selected histological subtypes of the tumors. Therefore the WHO initiated very early an international case-control study (Interphone Study) with a common core study protocol. The first articles based on this study protocol were published on the basis of the national data of Danish and Swedish Interphone Study groups (Christensen et al., 2004, Lönn et al., 2004, Lönn et al., 2005, Christensen et al., 2005). But still, the proportion of study participants using a mobile phone for 10 years or more is low.

A case-control study to mobile phone use and the risk for melanoma of the eye was performed in Germany (Stang et al., 2001). Among users of mobile phones an increased risk was observed. But the use of a mobile phone was assessed in an indirect way only. A second study with this topic is still on-going.

Up-to-now there exists only one important epidemiological study on other tumor sites which was performed in Denmark (Johansen et al., 2001). This retrospective cohort study is especially meaningful because of her high number of study participants and her representativeness of the general population. The explanatory power of the studies publishes up-to-now concerning cancer and mobile phone use is not sufficient to evaluate the risk of long term users and/or heavy users of

mobile phones taking into account the possible long latency period between exposure and disease. A much better evaluation will be expected by the pooled analyses of the Interphone Study.

Epidemiological research on neuro-degenerative diseases and other diseases are very rare and are based on occupational exposure with RF-EMF. A Swedish-Norwegian study including more than 11,000 mobile phone users revealed only minor differences on fatigue, headache or sensitivity to heat between users of analogue phones or digital phones. But for both types of phones a clear trend has been shown between the symptoms investigated and the frequency and of mobile phone use or the duration of calls, respectively. Other variables like occupational stress, etc. which could be an underlying cause for these symptoms as well have not been asked in detail. Therefore, a clear statement cannot be made (Oftedal et al., 2000).

In a survey Chia et al. (2000) analyzed 808 men and women concerning their health status and the use of mobile phones. The disorders investigated have been impaired vision (dysopia), perception disorders (here: paresthesia, the heat sensation on the face or behind the ear), fatigue, loss of memory, loss of concentration, dizziness and headache. A significant difference between the exposed group and the non-exposed group in general as well as according to a dose-response effect was found for headache only. An experimental Swedish-Norwegian study has shown a dose-response effect between health disorders like headache, fatigue and perception disorders , and the frequency of mobile phone use and the duration of calls, respectively (Mild et al., 1998).

The findings of the few studies on mobile phone use and traffic accidents are in concordance. Accordingly, the use of a mobile phone while driving increases the risk of having an accident independently of the use of a hands-free device. These findings argue more for an effect of distraction than for a biological effect of the RF-EMF exposure (Schüz et Michaelis, 2001).

Up-to-now insufficient scientific knowledge on possible adverse health effect of mobile phone use, especially those of long term effects and of frequent use have led to an extreme controversy opinion in the scientific world, as well as among politicians and in the general public.

In view of the wide spread usage of mobile phones – there are more than 65 millions of mobile phone users in the Federal Republic of Germany – and its potential adverse health effects it is urgently needed to close this gap in scientific research.

As there is no known biological mechanism concerning RF-EMF exposure by mobile phone use epidemiological research is of paramount importance.

Using epidemiological methods it is possible to find changes in the occurrence of diseases, symptoms, or disorders in groups more exposed to RF-EMF. Certainly, epidemiological studies show correlations between risk factors and the diseases under investigation only, and are sometimes hardly to explain without knowing a pathogenetic mechanism. On the other side, experimental research is often triggered by epidemiological findings. Within a population it is epidemiology only which allows a reliable estimation of the attributable risk.

Short Description of the Project

Aim of the feasibility study was to evaluate if and under which conditions a prospective cohort study on mobile phone users is feasible within an international collaboration. The application areas defined by the Federal Agency for Radiation Protection (BfS) will be described in the following chapters.

In general, the approach to the planned cohort study had to be coordinated with the international study group which consists of scientists from UK, Sweden, Denmark and Finland. Within the frame of the feasibility study instruments for data collection and strategies of investigation given by the BfS had to be tested. The feasibility study should also include a pilot study with a sample of at least 1,000 people.

The project was divided into various sub-projects in order to test the feasibility of the prospective cohort study in the Federal Republic of Germany.

Firstly, a co-operation with the four net providers had to be established in order to randomly draw a sample of study participants stratified by exposure and age from their data files. If this turned out to be impossible other options of recruiting study participants had to be found and tested. Furthermore, it was required to get the data of incoming as well as of outgoing calls from the databases of the net providers. In order to do so it was necessary to check the possibilities to access the database and to check the structure of the data.

Secondly, the international questionnaire had to be translated into German and to be checked on its contents and feasibility. Possible as well as necessary modifications had to be done. A short questionnaire for non-responders had to be developed as well. A validation of data of exposure which should serve for selection of the participants out from the data base of the net providers had to be developed. This validation should be used in the course of the cohort study as well.

Thirdly, the possible data sources (cancer registries, registries for coronary heart diseases, clinic discharge registers, etc.) had to be identified and checked on their completeness and their accessibility.

Ethical issues and logistical issues concerning the prospective cohort study had to be evaluated in this feasibility study.

In the following, the experiences made within this feasibility study concerning the set-up of a cohort, the assessment of exposure data (mobile phone use), the questionnaire (exposure and disease), the follow-up of study participants, the conduct of the pilot study, the calculation of the statistical power of the study, and the cooperation within an international group will be presented briefly.

Conclusions from the feasibility study

The following issues have been identified as important:.

- The contact was established successfully with the net providers in order to check the recruitment of the cohort and the supply of exposure data.

Result: Cooperation with the net providers is possible in order to recruit the cohort and to get the exposure data.

- The legal data protection issues have been addressed on a state level as well as on a federal level. They have been incorporated in the study.

Result: The federal data protection law for telecommunication leads to restrictions of the planned study concerning the selection of study participants, the method of addressing them, and the collection of the exposure data from the data bases of the net providers. A modified procedure is possible.

- Statistical programmes for data selection, data bases, letters to participants and written informed consent have been developed.

Result: These instruments have been developed in a way to use them immediately in the planned prospective cohort study. A check by the data protection agency and the net providers was made and permission to use them was given.

- Establishing of the cohort stratified by gender, age and exposure using the files of the net providers was examined.

Result: Selection of participants using the data bases of the net providers is possible with the given stratification variables.

- Collection of exposure data from the net providers was examined.

Result: Yearly extraction of the data to mobile phone use of a three month period from the data bases of the net providers is technically possible and can be provided if informed consent of the study participants is given.

- Two projects have been carried out in order to get new knowledge concerning the parameters of power output of mobile phones under regular conditions.

Result: The collection of the first base station contacted is not needed for a better exposure estimation.

- Follow-up of end points (diseases) was evaluated.

Result: Mortality data can be collected using death certificates. Morbidity data for cancer can be provided by cancer registries. Clinic discharge registers are not always complete and are usually not population based. Therefore, for data collection on all diseases beside cancer as well as on adverse health effects a questionnaire is necessary

- Statistical power calculations in addition to those done in the UK have been performed.

Result: The international prospective cohort study will be able to detect small increases of risks even in rare diseases.

- A pilot study addressing 5,000 people was performed.

Result: Experiences have been made to conduct this study with the inclusion of the net providers as well as without them. Both approaches are possible, but each procedure has its cons and pros. In total, the response rate is rather low using either procedure which makes the set-up of a cohort very costly.

- The cooperation with the international study group which consists of scientists from UK, Sweden, Denmark and Finland was successful.

Result: The international study protocol was finalized in June 2005, as well as the international questionnaire which can now be adapted to national requirements.

Recommendations:

In order to give recommendations the advantages of a prospective cohort study with mobile phone users have to be understood. The following tissues will give an overview.

- Data on the exposure will be collected before the disease arises. Therefore, the disease can not bias the collection of the exposure data.
- It is possible to investigate various end points (diseases, adverse health effects). It is also possible to add more end points to the study protocol during the conduct of the study if sufficient scientific evidence is given.
- It is possible to adjust the collection of exposure data to the development of new technologies.
- The statistical power increases with the duration of the cohort study.
- With this study a surveillance system will be implemented in order to accompany a wide spread technology and its possible adverse health effects in a scientific way.
- In the course of this cohort study additions are always possible, like nested case-control studies and other investigations.

Because of the design of this study, i.e. the inclusion of mobile phone users only, the comparison of heavy users with light user will be possible. The possibility to get exposure data directly from the net providers will insure the quality of this study and, therefore, enhance its meaningfulness. Furthermore, this data can be used to validate the data given in the questionnaire.

Because of the indented long term schedule of this study also small increases of risks of diseases with long latency can be shown.

Another advantage of this planned cohort study lies in the international cooperation and the possible overall study size with its powerful meaningfulness. Germany can profit of the experiences of the other participating countries. Joint institutions can be set up, like a center for data management and analyses, which leads to reduction of overall costs.

Disadvantages of this prospective cohort study are the huge amount of money needed to establish this cohort, to alter the study protocol in order to make up for changing exposures, to establish an active follow-up to getting the defined end points correctly and completely, to control migration in order to avoid a high loss-to-follow-up.

Nevertheless, this feasibility study has shown that it is possible in general.

To establish the cohort using the data bases of the net providers is possible. The study participants can be drawn stratified by gender, age and exposure. The disadvantage of this procedure was the rather small response rate. As long as it will not be possible to identify the cohort study as a research project of public interest in the invitation letter, the response rate will remain low although it might be increased by alerting the public by accompanying media campaigns.

To establish the cohort using the general public with stratification by age and gender is possible as well. The proportion of heavy users was much better than expected as could be shown in the pilot study using this method. Although the response rate is higher compared with the mailing of the invitation letters by the net providers it is still relatively low. Additionally, it would have the advantage to include never users into the cohort as a baseline for comparison.

To evaluate the feasibility including financial aspects was not part of the feasibility study. Because of the low response rate yielded with both methods of addressing the possible study participants expenditures will be tremendous. However, the feasibility itself is not touched by this.

By restricting the study to suitable study regions, i.e. those with cancer registries, study participants with cancer can be ascertained easily. Anyway, an active follow-up will be necessary for all other end points. According to the experiences gained in this feasibility study the inclusion of the states of Rhineland-Palatinate and Saarland into the overall study region is recommended as in these states part of the needed infrastructure is already available.

The international questionnaire has to be used for the exposure ascertainment. The data of the net providers can be used for validation. Regular follow-up using a questionnaire is recommended.

Conclusion: All essential aspects of the international study protocol can be used in Germany. Although some procedures might be more complicated and, therefore, more costly, the feasibility itself was successfully demonstrated.

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