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An international prospective cohort study of mobile phone users and health (Cosmos): Design considerations and enrolment☆

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ABSTRACT

Background: There is continuing public and scientific interest in the possibility that exposure to radiofrequency (RF) electromagnetic fields (EMF) from mobile telephones or other wireless devices and applications might increase the risk of certain cancers or other diseases. The interest is amplified by the rapid world-wide penetration of such technologies. The evidence from epidemiological studies published to date have not been consistent and, in particular, further studies are required to identify whether longer term (well beyond 10 years) RF exposure might pose some health risk. *Methods*: The "Cosmos" study described here is a large prospective cohort study of mobile telephone users (ongoing recruitment of 250,000 men and women aged 18+ years in five European countries – Denmark, Finland, Sweden, The Netherlands, UK) who will be followed up for 25+ years. Information on mobile telephone use is collected prospectively through questionnaires and objective traffic data from network operators. Associations with disease risks will be studied by linking cohort members to existing disease registries, while changes in symptoms such as headache and sleep quality and of general well-being are assessed by baseline and follow-up questionnaires. *Conclusions*: A prospective cohort study conducted with appropriate diligence and a sufficient sample size, overcomes many of the shortcomings of previous studies. Its major advantages are exposure assessment prior to the diagnosis of disease, the prospective collection of objective exposure information, long-term follow-up of multiple health outcomes, and the flexibility to investigate future changes in technologies or new research questions.

1. Introduction

There is extensive public and scientific interest in the possibility that exposure to radiofrequency (RF) electromagnetic fields (EMF) from mobile telephones or other wireless devices and applications might increase the risk of certain cancers and/or other diseases. This concern is amplified by the rapid world-wide penetration of such technologies. Current exposure guidelines have been developed to minimise the effects of tissue heating from exposure to RF, which to date is the only known biological effect [1]. In a recent risk assessment by the European Commission it was concluded from three independent lines of evidence (epidemiological, animal, and in vitro studies) that exposure to RF below these exposure guidelines is unlikely to lead to an increase in cancer. However, as the duration of

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widespread exposure to RF is shorter than the typical induction time of some cancers of up to several decades, further studies are required to identify whether longer term (well beyond 10 years) RF exposure might pose some cancer risk [2]. For diseases other than cancer, few studies are available and the evidence is inconclusive. In the light of an absence of any credible biological hypotheses and convincing experimental results on how low-level RF could cause disease, epidemiologic research is particularly important. It is also the most relevant branch of science for risk identification and assessment because it directly investigates the putative exposure-disease relationship in humans under real-life circumstances.

The results of epidemiological studies on RF and disease risk published to date have not been entirely consistent, reflecting methodological differences and limitations, and hence the need for more rigorous studies [2–5]. To date the largest epidemiological study on the possible relation between RF and brain cancer has been the Interphone study. This study is a major collaboration comprising intracranial tumour case–control studies on RF exposure from mobile phones in 13 countries [6,7]. While there have been expectations that the Interphone study will provide answers as to whether mobile phone use is associated with increased brain tumour risk, it was already clear at the outset that it cannot address outcomes other than intracranial tumours nor induction and latency periods of more than about 10–12 years. Further limitations are the retrospective nature and quality of the self-reported assessment of mobile phone use that has been shown to lead to differential bias [8,9] and concerns regarding generalisability of findings due to the low response rates among control groups [10].

A large, prospective cohort study of mobile phone users with long-term follow-up has been given top priority in many EMF research agendas, e.g., by the World Health Organisation (WHO) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) of the European Commission. The design of a large multinational prospective study on health effects of a widespread and rapidly changing technology poses a number of challenges. We describe here the development of the protocol for such a study, recently launched in various countries across Europe, and named Cosmos (Cohort Study on Mobile Phones and Health). We also report here on experiences from pilot studies, expected and unexpected challenges before and during the launch of the study, and preliminary descriptive data of the national cohorts in Denmark, Sweden and the UK.

2. Study design

2.1. Study design and procedures

Cosmos is a large prospective cohort study of mobile phone users (aiming at 250,000 men and women aged 18+ years in five European countries – Denmark, Finland, Sweden, The Netherlands, and the UK) who will be followed up for 25+ years. Cosmos provides an epidemiologic evaluation of possible long-term health risks that might be associated with the use of mobile phones or other wireless technologies. These include risk of intracranial neoplastic, neurological and cerebro-vascular diseases, as well as changes over time in well-being and in occurrence of specific sub-acute and chronic symptoms, such as headache and sleep disorders. The prospective cohort design is well suited for such an investigation, because exposure information is captured prior to occurrence of disease, removing a major weakness of the previous case–control studies which are subject to possible recall bias. Information is collected prospectively on personal mobile phone use through questionnaires and objective traffic data from network operators. Incorporating data from operators minimises error and misclassification related to sole reliance on recall. The data being collected include number and duration of outgoing and incoming calls, technical features of the mobile phones and, in some countries, text messages, data transfer, and location of the first base station where the connection between handset and base station was made [11]. Additional information is obtained via questionnaires on past use of mobile phones, use of hands-free devices and the preferred side of the head where the mobile phone is used as well as use of cordless telephones, wireless computer networks, and other emerging RF technologies. In each country, traffic data is collected for each consenting participant, for a 3-month period annually. The questionnaire will be repeated periodically during the follow-up. The questionnaires are also used to assess medical history, potential confounders, e.g., smoking habits, alcohol consumption, education, and occupation, as well as health outcomes that are not routinely collected by registers, e.g., poor well-being and sleep disturbances. Population and health care registers will be used to acquire information on disease occurrence. Furthermore, some countries allow collection of other information such as use of medication from the prescription registers or residential history to assess whether study participants live close to mobile phone base stations or broadcast transmitters.

2.2. Health outcomes

No seemingly plausible biophysical or biological mechanism has been identified in relation to potential health effects of RF EMF. Therefore, the selection of health outcomes for epidemiological studies is based on the fact that the RF from mobile phones is mostly absorbed by the head, yet it includes the possibility that any tissue could be affected. Information on health outcomes is obtained from health care registers and questionnaires (Table 1). The combination of different sources of information offers flexibility in the selection of outcomes (i.e. facilitates the study of a wider range of outcomes compared with reliance on a single source of information) and enhances validity through ascertainment from several sources of information (increased comprehensiveness and level of detail). Information on cancer incidence and benign intracranial tumours is available for all national cohorts from population-based cancer registries. Information on occurrence of other diseases is available in Denmark, Finland, Sweden and the UK through hospital-discharge registers (also likely to become available in the Netherlands); these registers cover in-patients treated at hospitals in the entire country (outpatients included in Denmark). This is an important source of information for major diseases other than cancer that require hospitalization, e.g., cerebro-vascular disease. In some participating countries, national registers of specific diseases and medication reimbursements are available and can be used in the study; examples are for instance the Danish Multiple Sclerosis Registry (DMSR) and Finnish Social Insurance Institution. Routine registers of mortality by cause of death are available in all five participating countries. Assessing health outcomes accurately from disease registries is reliant upon the completeness and quality of those registries; while most of the registries to be used for Cosmos have a long tradition of registration and documented high quality, their quality still needs to be carefully monitored. For mortality and cancer incidence, follow-up will be almost 100% complete in each country. This is because once an individual has given their consent they can be followed up passively through registers. Only the health events of an expected small number of individuals who emigrate from their country or withdraw their consent will be unobtainable.

Questionnaires at baseline and at first follow-up planned after approximately 4 years will be used for assessment of changes in mobile phone use and other RF technologies as well as in health