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Midterm recruitment report. Recruitment applies only to the nested case control study

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D 5.3 Midterm recruitment report for the Case-Control study (Subtask 5.1.2)

The study documents (protocol, contact letters, informed consent, triptych and paper version of questionnaires) were prepared prior to being sent to the ethics committees. Contact with cases and controls could only be made after ethics approvals were obtained and collection of data could only start after participants had signed the informed consent forms.

Delays in obtaining the ethics approvals were due to:

- The 2-step approval process required in France. The Committee for Personal Protection (CPP) and the French National Commission on Informatics and Liberty (Commission Nationale de l'Informatique et des Libertés (CNIL) were both consulted as part of the ethics approval process.
- In Spain (and more specifically in Catalonia), first contact with the patients was planned to be performed by the Agency for Healthcare Quality and Evaluation of the Ministry of Health in Catalonia (AQUAS). All documents were reviewed by an AQUAS lawyer prior to being sent for ethics approval.

Delays in the implementation of data collection efforts were also associated with the preparation of dedicated questionnaires for the participants and their parents. Since the same questionnaires are used in the two participating countries, France and Spain, the questions and appropriate ways to address them were carefully selected to ensure adherence to cultural specificities.

The development of the online version of these questionnaires, which was done to avoid mailing and/or the involvement of interviewers, was impacted by technical issues, which resulted in delays of a few months. However, the well-designed database which is created directly from the questionnaire and filled-in, in real time by participants, assures high quality data collection that will facilitate data analysis at a later stage. It was determined that the questionnaires and associated database should be finalised, prior to any contact is to be made, so as to avoid a prolonged waiting period for the participants after they have signed informed consent forms.

First patients were contacted on 14 January 2019 (Month 20).

Although there were initial delays in contacting the participants, the implementation of the online questionnaire will allow for a faster response time by the participants. Collection of data, through the questionnaires, and of saliva samples, can thus be performed in a much faster manner than more traditional mailing and interviews (within about 8-12 months, depending on the response rate).

Status of data collection at mid-term (Month 30):

<u>Data collection in France</u>

Cases have so far been contacted via the following process:

- 34 letters were mailed to cases between March and June 2019.
- 7 letters were sent back due to an “unknown address”.
- Second mailings were sent out in September 2019.
- Follow-up contact by phone individually to be undertaken after a couple of weeks. Contact via phone numbers was unsuccessful for ~30% of the cases.

→ Overall, 3 cases have signed the informed consent forms.

The 3 cases have been invited to complete the questionnaire online (access codes have been provided) and to provide saliva samples. Contact with matched controls will be initiated at the beginning of 2020.

The possibility of contacting additional cases (and matched controls) will be investigated after completion of the follow-up study (Task 5.1.1).

Data collection in Spain

In Catalonia, AQuAs stopped the process of contacting cases and controls in April 2019, following the decision of the new director, despite its mission to generate relevant knowledge through the evaluation and analysis of data for decision making and the improvement of health. AQuAS stated that contacting patients was outside of its mandate.

In the following months, attempts were made to contact the patients (cases and controls) through the hospitals that performed their respective CT scans, or for cases, through their respective cancer treatment centres. We therefore:

- Contacted the 3 main paediatric hospitals to schedule in-person meetings with oncologists and radiologists
- Worked on all relevant documents for the contact cases (from oncology departments) and the contact controls (from the radiology departments), where for each set, a separate document was prepared to introduce the study either to children or adults
- Presented the requests for ethics approval in these 3 main hospitals, in addition to the requests to our ethics committee

→The same concerns were raised concerning the legality of medical doctors contacting the cases and controls, and approval was not obtained to send the letters from the hospitals.

Since September 2019, a new avenue is being investigated where it may be possible for the Director General of Planning in Health to take the responsibility of signing the letters. A meeting was finally organised on 21 November 2019 and a contract will be signed in the coming weeks so that letters could be signed by the Director General.

Assuming that the letters will be sent in early January 2020 (if not even earlier in December 2019), data collection will be completed in ~8 months, as cases and controls who are willing to participate, are anticipated to react soon after the receipt of the letters.

The case-control and follow-up studies (Task 5.1.1) will run in parallel in Madrid, where only a few cases have been identified.

We therefore anticipate meeting the revised deadlines in the new Grand Amendment by completing all data collection efforts by 30 September 2020 in month 40 of the MEDIRAD Project (MS33 – Case control field work completed – due in M40).