ERN-PAEDCAN Partner - Paediatric Rare Tumours Network - European Registry

(N°777336)

D4.2 - Report and recommendations on harmonized procedures of primary source data verification, registration and documentation

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This report is a part of the project 777336 PARTNER which has received funding from the European Union's Health Programme (2014-2020)

1. Introduction

The aim of the PARTNER project is to create a European Registry in order to prospectively collect data on children and adolescents (0-18 years) with very rare tumours. It was agreed that the European registry would have been created through the linkage of the existing national registries as “collaborative” structure that links national registries with the European Registry, in which the national data are transferred. This structure has several economic, regulatory and scientific advantages. Mainly, data quality can be controlled more efficiently through close connection with the treating hospitals on a national level and lack of language barriers.

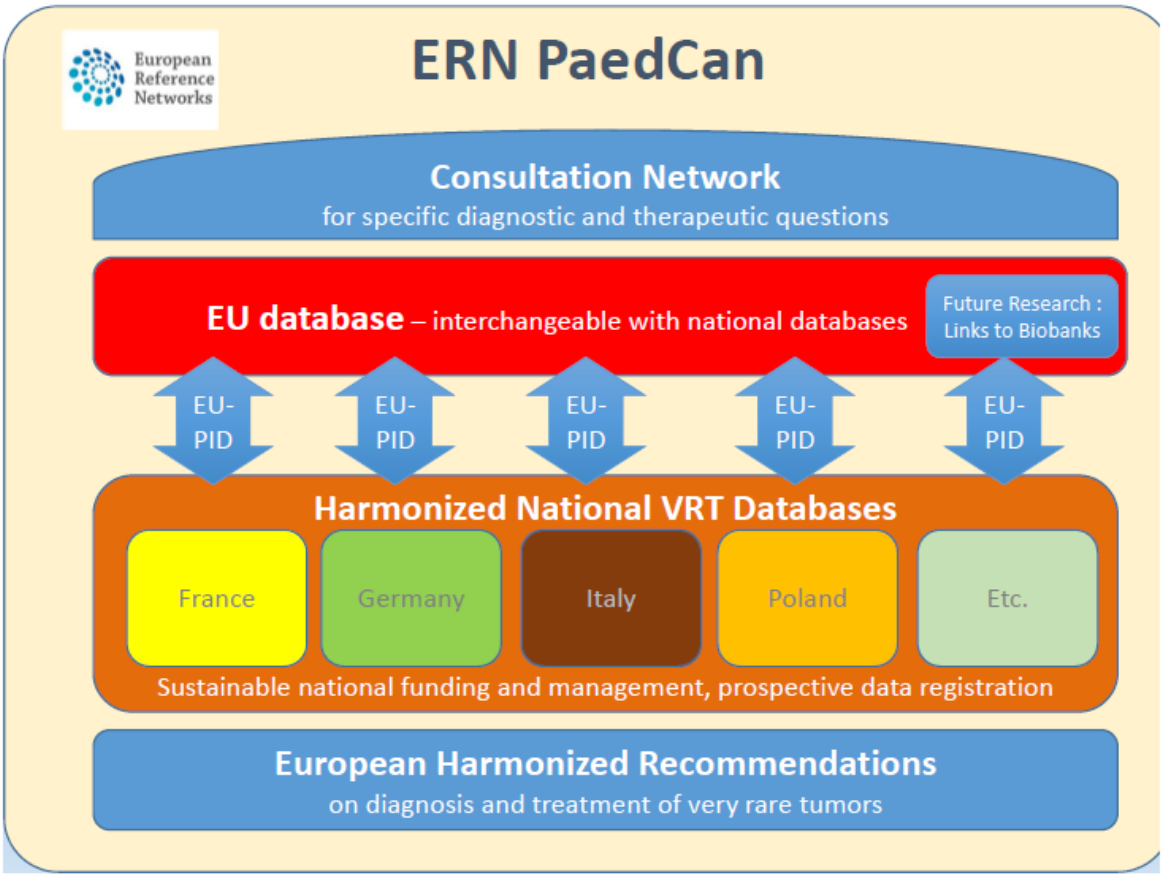

Figure 1: Structure of the planned European data base for rare paediatric tumours

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Detailed data on VRT have been collected over years into national registries within France, Germany (including Austria), Italy and Poland. There are existing established methods for primary data source verification, registration and documentation. Detailed national structures were reported within the Second Consensus Meeting held in Tubingen on June 7th, 2019.

2. Summary of national measurements for methods for primary data source verification, registration and documentation

The structures within the cooperating national registries in France, Italy, Germany, and Poland are different, however a consensus was reached in regard of measurements for harmonized procedures of primary source data verification, registration and documentation.

a) Eberhard Karls Universitaet Tuebingen, Ines Brecht – *The German data base and MARVIN*

The German Rare Pediatric Tumour Group is in the process of building a remote data entry data base (MARVIN, supported by GPOH – German Society for Oncology and Hematology), which will use EUPID and follow the agreement on entities and variables agreed on during the data harmonization process of the PARTNER project. So far, paper CRFs and an ACCESS data base were used. The CRFs were filled out by data managers at the cooperating treating hospital after consent of the patients. Afterwards the CRFs together with original reports were sent to the study center, where the documentation was checked for consistency with original data sources. In case of inconsistency the treating hospital was contacted. For each case tumor tissue is examined by a local pathologist as well as reference pathologists before registration in the data base.

b) Azienda Ospedaliera di Padova, Gianni Bisogno – *The Italian data base and CINECA*

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Documentation for patients into the Italian data base is done at study centre as well as data control. A remote data entry (CINECA) is currently being constructed under the AIEOP umbrella within CINECA. The registry will be adapted to the necessities of PARTNER. It is planned to use the EUPID for pseudonymization. Data quality measurements are applied including reference pathology.

c) Institute Curie Paris, Paris, Daniel Orbach – *The French Data base*

The French data base is presented (EPIDATA). This is a remote data entry data base, but there is no consistent control of data quality.

d) Gdansk University Medical Centre, Ewa Bien – *The Polish Data base*

The data base of the Polish Registry on Rare Pediatric Cancer (PPRTSG) has a central structure. Data documented at the study centre within an Excel Sheet by in the field experienced pediatric oncologists. Data quality measurements are applied including reference pathology.

In all countries consent of the patients to register within national data bases and data protection is ensured according to national regulations.

3. **Recommendations on harmonized procedures for primary data source verification, registration and documentation**

Existing national VRT registries may differ in many aspects: data are collected for different tumours, in different languages, in different ways, using different IT technologies. Moreover, the different registries are supported with varying and limited economic resources.

Harmonized procedures of primary source data verification, registration and documentation will ensure data quality. Regulations and published recommendations of the EU and different working groups were studied, e.g. Kodra et al. “Recommendations for Improving the Quality of Rare Disease Registries” 2018, experts will be involved. A

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list of duties for IT-partners will be created (MS 8). The discussion will be started at the Consortium Meeting in Brussels in January 2019.

Registration

Before registration of a patient in the PARTNER data base the diagnosis will be verified by a reference pathologist. Also the patient and/or his/her parents need to be informed about the aim of the registry, the type of personal information to be stored, the use of the data and how the data can be accessed and how consent can be withdrawn by the patient or his/her parents. A consent form has to be signed by both parents and/or the patient. Special consent is needed for international cooperation. The existing national consents need to be updated and re-submitted for verification of the the national ethical committees. Patients have to be kept updated about policies.

Only patients, who fulfil a number of **inclusion criteria**, can be registered with the registry. For this registry there are no exclusion criteria.

- “any solid malignancy characterized by an annual incidence < 2 cases/million and not considered in other clinical trials “
- Written consent, also for international transfer of data
- Age < 18 years

Primary source data verification

The PARTNER data base will be designed as a remote data entry base. Data will be entered by the treating hospital - physicians, study assistants or data managers. Tools for managing data quality through a system of plausibility checks and warnings will be integrated in the system. Importantly, original reports like operation reports, pathology reports, images, etc. will also be send to the national study centre, where data will be verified by the study physician. This method for data quality control is most important

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and needs to be done before final integration of data into the registry data base. Data quality audits may be used. Finally, data will be regularly analyzed by a statistician. Standardized reports may be used.

Documentation

An important measurement for data quality was the harmonization process of the project. In all registries the same information is collected on a core set of entities using a core data set. The same variables, classifications, coding systems and terminologies are used.
It is important to ensure to comply with the national and international ethical and legal standards. Confidentiality is insured on an operational level (pseudonymization, security measures), but also by training of study documentaries and physicians.

PARTNER needs to fulfil all legal requirements for data protection, most importantly 'The General Data Protection Regulation (GDPR)', which was officially applied across Europe on 25 May 2018. Patients' data should be protected through encryption, secure communication channels shall be used and strong authentication.

1. Each national registry has its own procedures to guarantee privacy in data protection. Methods need to be adapted in order to fulfil the requirements by European law.
2. The PARTNER project will include the EUPID system, a privacy-preserving system for pseudonymous patient registration and record linkage that has been developed in a previous EU funded project
3. The IT provider that will be identified to build the EU VRT Registry structure (see WP5) will be asked to own all the necessary procedures and certifications to guarantee data protection and privacy

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It is of major importance to ensure follow-up information on patients. This is critical for calculation of survival curves and analyses of data using univariate and multivariate analyses. Through many cases with “lost follow-up” a bias may be generated. Therefore, long term-funding is needed in order to ensure long-term sustainability.

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