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The Portuguese National Registry for Hemophilia: Developing of a web-based technological solution

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Abstract

The crucial role that patient records have in the management of the rare and chronic diseases greatly increases the need to create mechanisms to facilitate the identification and management of the patient's data. Hemophilia is an X-linked congenital bleeding disorder caused by a deficiency of coagulation factor that affects the population on a ratio of 1 case for 10,000 people born. Currently, there are several countries with technological platforms to support the National Patients' Registries (NPR) of Hemophilia and other Congenital Coagulopathies (HoCC), due to its benefits in the management of the disease. This work presents the technological platform developed in a joint initiative between the University of Aveiro (UA) and the Portuguese Association of Congenital Coagulopathies (PACC), with the purpose of creating the first NPR with HoCC in Portugal. This web application is hosted in the data center of the University of Aveiro, and is being used by the clinicians of the different Hemophilia Treatment Centers (HTC) across the country.

Keywords: National Pacients Registry, Web-application, Hemophilia, Congenital Coagulopathies

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1. Introduction

According to the report of the World Federation of Hemophilia (WFH), an important measure for improving the management of Hemophilia and other Congenital Coagulopathies (HoCC) is the existence of patients' registries, which, in a national context, could lead to the National Patients' Registries (NPR) with HoCC [1]. The vision of the WFH with 'Treatment for All' is that all people that suffer with HoCC must have access to medical care and appropriate treatments. For this, the identification of all patients who suffer with this disease represents the first step, being the NPR the fundamental tool for such identification [2].

Registries of patients have the invaluable potential to provide an understanding of the disorder, to provide useful information for planning health care services and to identify suitable groups of patients for clinical trials enrolment [3]. This kind of registries are particularly useful for people suffering with rare and chronic diseases, such as HoCC, where important research questions cannot be answered without a set of information about the prevalence and evolution of the disease. Registries for rare diseases are broadly accepted for their usefulness in monitoring the identification and diagnosis of people with hemophilia (PWH) and evaluating their health.

The purpose of a Registry in the context of HoCC is to define the population demographics and collect observational data on specific hemophilia health concerns such as the prevalence of viral infections, factor inhibitors, implementation of prophylaxis, and track the usage of the products (drugs).

In addition to the demographic characterization of the population with hemophilia, the existence of those records allows the collection of data for statistical analysis related to the specificity of the disease, such as the prevalence of viral infections, existence of inhibitor factors, implementation of prophylactic treatments, joint evaluation, among other mechanisms to assist the decision making process.

Given the importance of these data for disease management, the consistent definition of this data, its correct storage and possibility of subsequent extraction of information are important factors for a more objective view of the practice of hemophilia care, with a profound impact on the health and in the quality of life of these patients.

The lack of a National Patients Registry for Hemophilia and other Congenital Coagulopatias in Portugal, associated with the difficulty that clinicians of this area faced in order to manage the specific patient information, motivated a group of physicians to seek for a technological solution that facilitated and optimized the information management process.

This article presents the newly developed web-based solution to support the Portuguese National Hemophilia Registry, whose project arose from a joint initiative between the hemophilia healthcare professionals, represented by the Portuguese Association of Congenital Coagulopathies (PACC) and a group of researchers from the University of Aveiro (UA) responsible for analyzing, developing and implementing the technological solution.

2. Registry and its role in chronic and rare diseases

Registry is defined in epidemiology as a data file with information efficiently recoverable, related with elements that are important for health in a defined population in such a way that the registered elements can be extrapolated to a base population [4]. In the scope of congenital bleeding disorders, the registry is a database of people identified with this disease including information on personal details, diagnosis, treatment and complications [1], [5]. The registry is thus a key tool for identifying and tracking individuals with a particular disease, and consequently for quality control and quality assurance in treatment, and for studying the impact of new developments on prevention, diagnosis and treatments [6].

These registries contain demographical, social and clinical data, categorized in diagnose, treatment and follow-up data. The WFH recommends that this data be stored in a centralized unique national repository, as, among other benefits, avoids patient duplication, ensuring a greater reliability of registries in order to portray a faithful reality of the disease in a country [1]. Given the usefulness of these systems, there are several countries that have already implemented NPR in the context of Hemophilia and other Congenital Coagulopathies. Considering the results the results of a study published by O'Mahony *et al.* in 2012 [7], that was based in an inquiry made in 35 European countries, there are 27 countries with NPR and 8 without a NPR, a group where Portugal was included.

In the countries with a NPR, not all have the information openly available, and some of them are reported in the literature, as the NPR from Austria [6], Italy [6], Spain [8], Poland [9], Switzerland [10], United Kingdom [11],

Germany [12]. Other NPR are referred in the work of other authors as is the cases of NPR from Bulgaria, Czech Republic, Slovenia, Finland, Greece, Russia, and Slovakia [7]. Outside European continent, there are other reference NPR in this area, as is the case as the NPR from Canada [13].

3. The Web-application to support the Portuguese National Registry for Hemophilia

This work aims to present the web-application to support a National Registry of Hemophilia and other Congenital Coagulopathies in Portugal. The analysis, conception and development of the platform that would support NPR with HoCC in Portugal was a joint initiative between the Portuguese Association of Congenital Coagulopathies (PACC) and a group of researchers from the University of Aveiro (UA).

The PACC is a non-profit organization represented by a group of health care providers in the area of HoCC, and the entity responsible for defining the rules, guidelines and setting goals for the NPR.

The University of Aveiro was the part responsible for the technology leadership, more specifically for the analysis, conception, implementation and maintenance and support of the NPR of HoCC platform.

3.1. Disease characterization and problem contextualization

Hemophilia is an X-linked congenital bleeding disorder caused by a deficiency of coagulation factor [2]. According to the WFH's annual global surveys, the number of PWH in the world is approximately 400 000, affecting the population in a ratio of 1 case for 10,000 people born [5].

Portugal is a country with 10 million inhabitants and about 1000 PWH are expected. However, the number of the other cases with Congenital Coagulopathies, including the vonWillebrand disease (vWB) and other type of deficiencies of factors, does increase this value. To treat these patients, there are different treatment centers scattered through Portugal, and despite the efforts and recognition of the need of a NPR, just recently the protocol for the creation of the system to support the Registry was approved. For this project, the establishment of an expert working group was endorsed, involving a group of physicians and a group of researchers in the field of computer science, aiming to develop the first Web-based platform to support the NPR for HoCC in Portugal.

3.2. Methodology of Development

The development process of the web-platform (named *hemo@record*) followed an iterative and incremental process, which allowed the requirement elicitation and its validation with a group of clinicians, future users of the system [14]. Information collected in this phase was incorporated into a detailed specifications document to guide development, using an object-oriented (OO) environment.

After this phase, a detailed description of the registry was submitted to the National Committee for Data Protection in March 2013 and consent for the registry was obtained two months later. The guidelines of the National Data Protection Agency on confidentiality were carefully followed along the development process of the technological solution and the web-based application that supports the NPR for HoCC in Portugal is operated and maintained in accordance with the Data Protection Law. The data will be collected in the application after consent of the patient.

3.3. Brief Description of the technological solution developed

The *hemo@record* was developed to store and manage a set of anonymous data from patients with HoCC, and to be used by clinicians that treat people with this disease scattered over the country. There are two different profiles of users (actors) with access credentials to use the system, namely:
- Physician - it includes the doctors that treat PWH and have permission to perform a set of tasks, including introduction, update, deletion of their patient's data, as well as, query and visualize information (with some critical data hidden), from all the patients at national level;
- Coordinator – it is also a doctor with administration permissions, having access to all the functionalities of the system.

Each patient has his/her personal data hidden and is identified by an anonymous code, having associated a set of records that reflects his/her clinical history in terms of health through time. To provide an efficient set of functionalities to the users, the system is organized through a set of 8 modules, managing demographic, clinical and treatment data (see Fig.1).

Fig.1 - Snapshot of modules present in hemo@care (user interfaces in Portuguese).

- ▪ Two of those modules are statistical modules, presenting a set of statistical indicators, at national and local level;
- ▪ Six modules providing data management functionalities (insert, update, delete, export): Modules for administration and audit purposes (available to the coordinator only), and modules for patient management, registry management, treatments management and death management.

Modules to visualize national and local statistics

The national statistics module was designed to present a set of national indicators, reflecting the current situation, encompassing the data from all the patients introduced in the system by their doctors. These indicators provide a complete analysis of the national situation, namely: (i) distribution of patients per area of residence; (ii) distribution of patients per Hemophilia Treatment Center (HTC) or Hospital; (iii) distribution of patients per type of coagulopathy; (iv) distribution of patients per type of treatment; (v) distribution of patients per severity of disease; (vi) distribution of patients per treatment regimen; (vii) evolution in the number of occurrences; and, (viii) evolution in the number of deaths.

The local statistics module presents the same indicators, with the exception of those that identify the geographic location of the patient, such as: 'distribution of patients by place of residence' and 'distribution of patients per HTC or Hospital (see Fig.2)

Fig.2 - Snapshot of user interface with indicators of local statistics module (interfaces in Portuguese).

In a nutshell, the difference between these two modules is that the former present all the national data, while the later only presents the local data associated with the user HTC. Each statistics module is presented in a specific chart (pie chart, bar chart, etc.) that is appropriate to the type of data that is provided by the module (see examples in Fig.3).
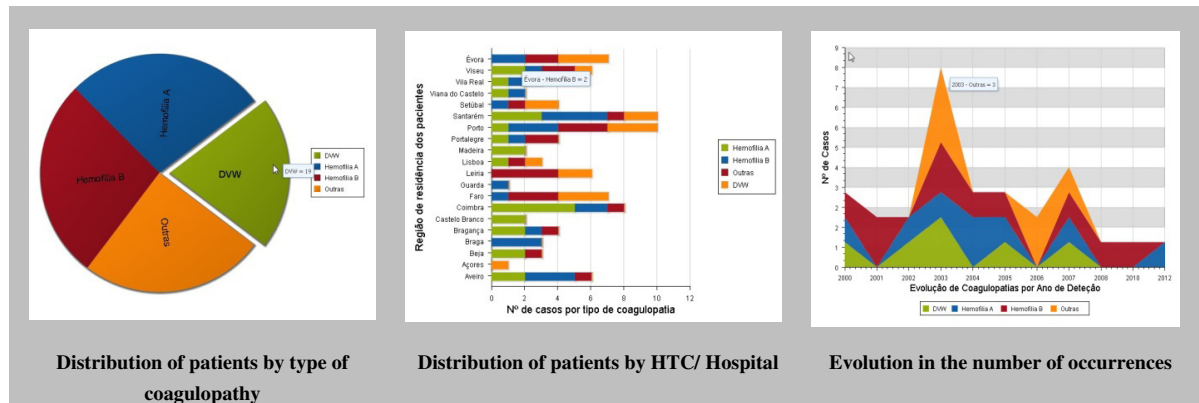

| Distribution of patients by type of coagulopathy | Distribution of patients by HTC/ Hospital | Evolution in the number of occurrences |

Fig.3 - Snapshots with examples of some indicators (in Portuguese with fictitious data).

Modules to manage patients' data

The remaining six modules provide the information to manage all patient data. The first step to use the web-application is the introduction of the patient basic data, i.e., the anonymous and unique patient code, complemented with a set of demographical data as gender, HTC or Hospital, data of birth, place and country of birth, and place and country of residence, (Figure 4 - left side). The patient is introduced only once, the system having an automatic process that identifies possible duplications, triggering automatic mechanisms for alerting the Coordinator. After registering the patient, it is possible to introduce registries for that patient. Each registry stores the patient's health condition at a specific instant of time, more specifically the clinical condition or/and the social and life quality information. To be able to assess the evaluation through time, each time a change on a given situation or medical condition occurs; the system automatically creates a new record. As such, each patient can have several registries, and through the analysis off all the records, is possible to determine the evolution of the patient's health condition, social and quality of life evolution.

The system presents patients listings in a proprietary grid view, using a color representation in order to promptly identify different situations, like patients without associated registries, patients that belong to the same HTC as the physician, patients already diseased, etc. (Figure 4 - right side).
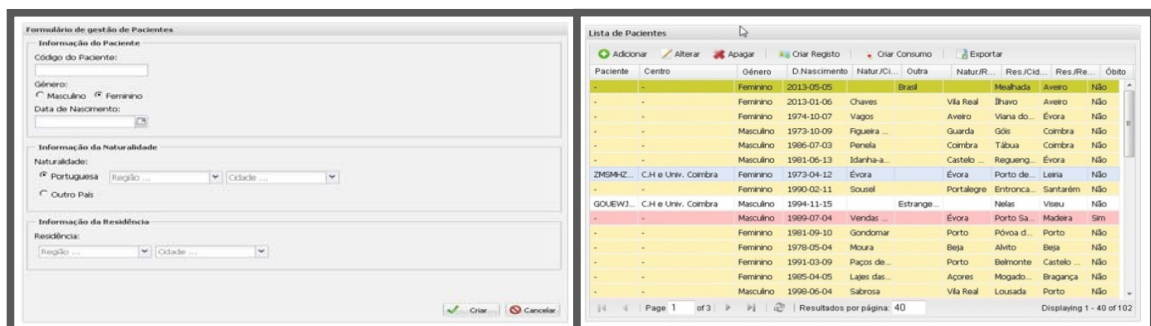

Fig.4 - Snapshot of some aspects of the user interface (in Portuguese with fictitious data).

Due to the laws of privacy and data protection, the identifying data of patients from other HTC's (anonymous code and hospital name), are hidden. As can be seen in Fig.4 (right side), there are several functionalities that can be performed after selecting a patient, such as: create or update patient's registries, create or update patient treatment details (treatment date, drug name and consumed dosage). To facilitate the statistical analysis and detect trends, the data can be exported to a Microsoft Excel format for posterior analysis. All the grids provide powerful filter and sorting mechanisms, having each field a specific filter system adapted to the type of data hosted in that field (for example, a date field allows to filter dates within a chosen interval, etc.).

The system also provides a complete solution to manage the details of the patient treatments, according to the rules imposed by the WFH such as: create or update data about Coagulation Factor Concentrate (CFC) products (drugs used in Hemophilia treatments), create or update suppliers, create or update patient consumption details, etc. Fig.5 (left side) presents the example of interface that allows to record a patient's treatment details, while Fig.5 (right side) shows all the treatments presented on the system proprietary grid, providing the same powerful filtering and sorting mechanisms.
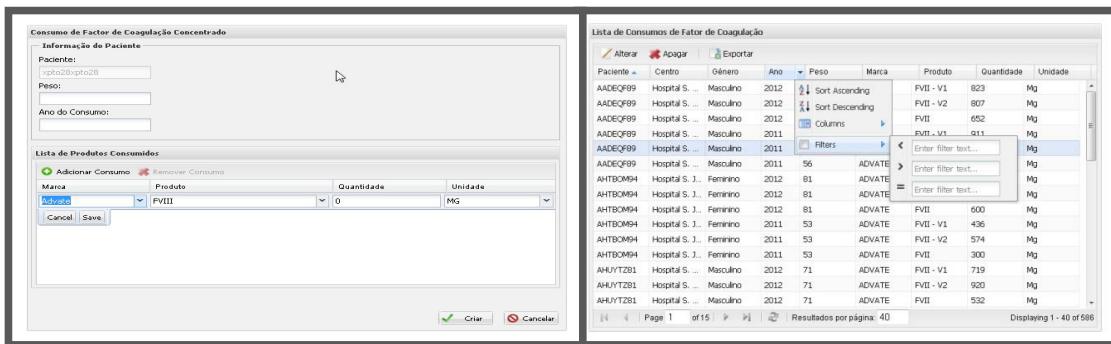

Fig.5 - Snapshot of some aspects of the user nterfaces (in Portuguese with fictitious data).

3.4 . Technological Solution

From a technological standpoint, the *hemo@record* web-application was developed using the Spring development Framework, a Java platform that provides comprehensive infrastructure support for developing Enterprise Java applications [15]. The advantage of using the Spring framework is that it handles the infrastructure support details, allowing developers to focus on the business logic of the system. The Web frontend was developed using Sencha GXT, a Java-based framework for building feature-rich web-applications based on GWT. "GXT features high-performance user interfaces (UI) widgets that are interoperable with native GWT components, templates, and layout manager" [16]. GWT is a development toolkit for building and optimizing complex browser-based applications. Its goal is to enable productive development of high-performance web- applications without the need to be an expert on web technologies such as HTML, JavaScript, CSS, etc. Using GWT, the cross-browser inconsistency is eliminated, as GWT compiles a specific version optimized for a specific browser. The Data Base Management System (DBMS) used was Oracle MySQL.

In order to avoid the complexities of the underlying Data Base Management System (DBMS), and, if needed, to easily swap the DBMS used, an Object/Relational Mapping (ORM) framework was used. Hibernate is an ORM framework that allows the use of natural Object-oriented idioms including inheritance, polymorphism, association, composition, and the Java collections framework to manipulate database data [17].

The *hemo@record* runs on an Apache Tomcat Web server, an open source software implementation of the Java Servlet and JavaServer Pages technologies. In a nutshell, each use-case of the web-application generates a request that is processed by the server that runs in specific business logic, retrieves the requested data from the *hemo@record* database, transforming the data in Java objects by the use of the ORM framework. These objects transport the data extracted from the database, and are returned to the web-application. The browser that renders the web-application

interprets the data, using the compiled GXT widgets to present it as useful and relevant information for the end user.

4. Conclusions

The use of Information and Communication Technologies (ICT) in rare and chronic disease have shown numerous advantages in terms of data management and information retrieval, with great impact on the quality of health care provision, research and public health monitoring trends. In the context of hemophilia, several countries had already taken advantage of ICT, implementing technological solutions to support the National Registry of Patients. Portugal is a small country with about 10 million inhabitants and 1000 expected PWH. Despite the fact that the national patient registry is a desire project from several years, the protocol for the creation of an online national registry was only recently signed, involving a group of healthcare professionals, represented by the PACC and a group of researchers from the University of Aveiro.

This paper described a web platform that supports the National Patients' Registries (NPR) of Haemophilia and other Congenital Coagulopathies (HoCC) in Portugal. This recently created platform (*hemo@record*) allows a complete solution for managing the complexity of data associated to Haemophilia and Congenital Coagulopathies patients, including clinical, social and health status monitoring data, thus reflecting in real time the national reality in terms of HoCC data. As such, the *hemo@record* can give answer in real time to questions such as: 'How many?', 'Where are they?' and 'How are they?' assuring a proper and informed treatment, provided by clinicians of the several HTC from all over the country.

Acknowledgments

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