The HemoRec Database as an Example of a Rare Diseases Registry

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Abstract

Rare diseases constitute a major burden on public health, mainly due to the high cost of therapy and logistical difficulties (for example, the need to organise a network of designated treatment centres). National and international registries of rare diseases facilitate data collection and analysis for demographic, economic and research purposes. They are also useful for treatment centres and other healthcare providers and pharmaceutical companies developing orphan drugs. We present the HemoRec database, implemented in 2006 in six European countries, as an example of an international registry of inherited bleeding disorders. HemoRec is used in 15 Polish treatment centres and stores data on 1,100 patients with inherited bleeding disorders (amounting to 24.9% of all patients registered in the Polish central registry held at the Institute of Haematology and Blood Transfusion in Warsaw). It can be developed in the future into a national platform of data collection and exchange in the network of Polish, and hopefully also European, haemophilia treatment centres.

Keywords

HemoRec, haemophilia, registry, rare diseases, orphan diseases, bleeding disorders, rare bleeding disorders, von Willebrand disease

Disclosure: The authors have no conflicts of interest to declare.

Acknowledgements: The HemoRec database was created and maintained within an unrestricted educational grant from the pharmaceutical company NovoNordisk A/S. We would like to acknowledge all those who participated in the development of this database in Poland through entering the data of patients in haemophilia treatment centres: Mariola Bober, Halina Bobrowska, Radoslaw Bogucki, Grzegorz Dobaczewski, Arkadiusz Drobiecki, Magdalena Gorska-Kosicka, Anna Janik-Moszant, Pawel Laguna, Jaroslaw Peregud-Pogorzelski, Dorota Siminska, Ewa Stefanska-Windyga, Jacek Trelinski and Ewa Zuk.

Received: 9 November 2010 **Accepted:** 15 March 2011 **Citation:** *European Oncology & Haematology*, 2011;7(2):147–50 *DOI: 10.17925/EOH.2011.07.02.147*

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Adequate and thorough patient data collection and management is an integral part of every modern healthcare system. Well-designed, easily accessible and secure databases are needed, particularly in the field of rare, inherited, chronic diseases that generate high economic burdens on healthcare systems. Depending on the structure and functionality of the registry, it can provide valuable data on the prevalence, clinical picture and treatment of the disease, enable constant verification of the demand on therapeutic options (usually orphan drugs) and the monitoring of adverse events.

Rare diseases are usually defined as conditions affecting fewer than five per 10,000 persons.[1] According to the US Office of Rare Diseases Research, a rare disease (or an orphan disease) is a condition affecting fewer than 200,000 persons (www.rarediseases.info.nih.gov). Several thousand rare diseases fulfilling these criteria can be identified, and they affect approximately 3% of the whole population.[1] Congenital bleeding disorders are also included in this list, as their prevalence does not exceed 1:10,000 for haemophilia,[2] 1:250,000–1:1,000,000 for type 3 von Willebrand disease[3] and 1:500,000–1:2,000,000 for other clotting factor deficiencies.[4]

Most rare diseases are genetically determined, severe, debilitating conditions. Efforts to collect data and create registries of these disorders are being constantly made in order to facilitate treatment, research, demographic analyses and drug development.[1,5,6] Moreover, increasing the number of patients can significantly improve the quality of research in the field of rare diseases. A recent initiative of the Office of Rare Diseases Research, launched at the workshop held in Bethesda, Maryland, US on 11–12 January 2010, underlined the need for a central registry collecting core data from different databases across the world and addressed the matter of data control and access.[5] European projects concerning rare diseases include the Orphanet database, designed in France in 1997 and which spread to the whole of Europe in 2000 (www.orpha.net), the Rare Diseases Task Force, funded by the European Commission Public Health Directorate in 2004 (www.rdtf.org) and the European Organisation for Rare Diseases (EURORDIS) – the patient-driven organisation founded in France in 1997, which brings together 434 member organisations from 43 countries (www.eurordis.org). Prevention, diagnosis and optimal therapy of rare diseases are the main challenges highlighted by these projects. They are based on

the assumption that addressing the factors common to all rare diseases is more effective than looking at each particular condition separately. In this article we present the HemoRec database, established in Poland in 2006, as an example of a registry of rare bleeding disorders. It was implemented in selected treatment centres in the country and is being developed in order to collect data on inherited bleeding disorders and create the basis for data analysis and exchange between all relevant healthcare providers.

Registries of Inherited Bleeding Disorders

European Principles of Haemophilia Care, formulated in 2008 by a panel of experts,[7] stress the importance of collecting data on haemophilia and related bleeding disorders, and recommends that each country should have a national haemophilia patient registry. Most countries across the world use different kinds of local databases, usually led independently by particular haemophilia treatment centres (HTCs), and a central database, held by the leading HTC of the country. The history and the current status of the Polish registry of patients with inherited bleeding disorders was described recently.[8]

A large database of patients with inherited bleeding disorders was established in the US. The national surveillance programme, initiated in 1998, enabled collection of data on more than 26,000 patients with inherited bleeding disorders treated in 140 HTCs across the country (www.cdc.gov/ncbddd/blooddisorders/udc/).[6] This database provides valuable, constantly updated information on prevalence, demographics, treatment modalities and complications of haemophilia and von Willebrand disease in the US, published regularly in the form of reports.[9]

Several attempts were made to create global databases of particular bleeding disorders or treatment modalities. There are three international registries of immune tolerance induction in patients with haemophilia and inhibitors: the International Immune Tolerance Registry,[10] the North American Immune Tolerance Registry[11] and the ISTH-SSC FIX Inhibitor Registry.[12] In 1996 in Milan a large international project commenced, called the Rare Bleeding Disorders Database (www.rbdd.org), which aimed to extend the knowledge of the rarest bleeding disorders (clotting factor deficiencies except for haemophilia A, haemophilia B and von Willebrand disease). A similar database was created in North America in 1999.[13] There are also several independent international registries of patients with different factor deficiencies such as the Seven Treatment Evaluation Registry (STER), founded by the International Factor VII Deficiency Study Group (www.targetseven.org), and the Greifswald Registry of FX deficiency.[14]

The HemoRec Project

The international HemoRec project was initiated in 2006. Its aim was to improve the registry of patients with haemophilia with and without inhibitors in Central and Eastern Europe. The project has evolved over the past few years and now includes patients with other inherited bleeding disorders. The Iinternet-based application HemoRec was developed by the Institute of Biostatistics and Analysis at the Masaryk University in Brno, Czech Republic and implemented in the largest HTCs in the following countries: Czech Republic, Slovakia, Poland, Serbia, Macedonia and Latvia.

The HemoRec database and the HemoRec website are hosted by two servers owned by the Masaryk University in Brno. The Institute of Biostatistics and Analysis provides technical support (Help Desk), which is available 24 hours a day, for each HTC using the application. Availability of both host servers and of the database itself is 99.9%.

Sending confidential data via the Internet requires strict safety measures; therefore, data gathered in the database are managed in accordance with global data privacy regulations valid in the European Union (e-Privacy), in the US (21 Code of Federal Regulations [CFR] part 21, the Health Insurance Portability and Accountability Act [HIPPA]) and Canada (the Personal Information Protection and Electronic Documents Act [PIPEDA]). Patient data are anonymised and sent between HTCs in a password-protected and strictly encrypted manner (using 128-bit Secure Sockets Layer [SSL] certificates). Personal information on each particular patient is stored exclusively in the application of the original HTC and can be accessed only by designated healthcare professionals from this centre. Back-up copies of data stored in the database are preserved in a professional data centre.

The HemoRec database has a broad functionality. Demographic and clinical data can be collected and stored, including physical examination and medical history, results of laboratory tests, details in terms of bleeding episodes and treatment. Each stored parameter can be analysed and presented in the form of a graph, which is useful in creating reports and economic analyses, as well as estimating demand for clotting factor concentrates. Handling the application is straightforward and does not require expertise in dealing with advanced computer databases. Each physician authorised to access the database uses an individual login and password. The MyHemorec module enables registration of bleeds and usage of factor concentrate by the patients themselves in their home setting. It can also serve as a communication platform between the patient and their HTC/attending physician.

HemoRec can be used to design and conduct clinical trials. Research projects, individually adjusted to the specific needs of each centre or country, can markedly influence the quality of care and optimise therapeutic procedures in the field of inherited bleeding disorders. Possible areas of research include the assessment and comparison of treatment schedules or dosing,[15] the efficacy of prevention of arthropathy in patients on prophylaxis and the efficacy of physiotherapy. Data can be evaluated prospectively as well as retrospectively.

The status of the HemoRec database varies in each country. At the time when the project was started, a central/national registry was already held; therefore, in most countries, HemoRec serves as an independent registry of patients with haemophilia with and/or without inhibitors. In Serbia, HemoRec serves as a national patient registry and is used to monitor treatment, document the consumption of factor concentrates and estimate demand on these preparations by the Ministry of Health. In Macedonia it gained a similar status and became the national registry of patients with haemophilia.

Since 2006, 1,110 patients with inherited bleeding disorders have been registered in the Polish HemoRec, comprising 24.9% of all patients with inherited bleeding disorders registered in the Polish central registry, held at the Institute of Haematology and Blood Transfusion in Warsaw (status as of 2 November 2010). Fifteen HTCs located in the main cities of Poland have access to the HemoRec database: five paediatric and 10 adult (see *Figure 1*). A written informed consent for processing personal data was signed by each patient, in accordance with the Polish Personal Data Protection Act

(Dz. U. 2002 No. 101 item 926, as amended). The distribution of diagnoses is shown in *Table 1*, in comparison with the central registry. Data on bleeding episodes were transferred from home diaries of the patients. As of 2 November 2010, 4,895 bleeds were registered, occurring in 314 patients with haemophilia.

The current and future status of the HemoRec database in Poland was presented and discussed recently.[8] Currently, HemoRec is used in a very limited range, individually at each HTC and most commonly for research purposes. In the future, the database could be developed into an interactive platform of communication between patients and HTC workers. It can enable the supervision of home treatment, the dosage of factor concentrates and other aspects of therapy. It could theoretically be integrated with the national registry in the future or replace the current central database, offering much smaller technical capacities than HemoRec. Another possible development is the implementation of the database in the planned network of outpatient clinics for thrombosis and bleeding disorders as an electronic system of documentation. However, entering data into HemoRec and exploring further possibilities given by this database requires significant human and financial resources and good technical support and training.

Conclusion and Discussion

The need for well-designed, informative databases of rare disorders is clearly defined. Accurate and easily accessible data serve patients, physicians, researchers and pharmaceutical companies. The centralisation of information on rare disorders should be perceived not only on the national level, but also on the European level. International databases of rare disorders would facilitate and improve public health surveillance.

A good example of an international registry of rare diseases is the online database of primary immunodeficiencies led by the European Society for Immunodeficiencies (www.esid.org/esid_registry.php). Data collected in the registry enable research and contribute to the improvement of diagnostics, treatment and understanding of the mechanisms of these conditions.[16,17] HemoRec creates a good basis for a national and international database of haemophilia and related bleeding disorders. It already contains data on a representative group of patients with haemophilia and data on the vast majority of Polish patients with haemophilia complicated by the presence of factor VIII/factor IX inhibitors.

Recording all bleeding information (transferring it from the home diaries patients) would provide exact, prospective data on the usage of factor concentrates, frequency and localisation of bleeds and duration of treatment. The small number of bleeding episodes registered in HemoRec results from poor access to source data (individual paper diaries of the patients) and the time-consuming process of transferring the data to the database. The MyHemoRec module could facilitate these tasks, although it requires that the patient has a computer and Internet access.

In summary, we want to highlight the importance of regional and international registries, especially in the field of rare diseases. Launching the HemoRec project in Poland and other countries of the EU could be the first step to creating a modern, European database of inherited bleeding disorders, provided that adequate logistical and financial resources are allocated. ■

Figure 1: Polish Haemophilia Treatment Centres Participating in the HemoRec Project from 2006 to 2010

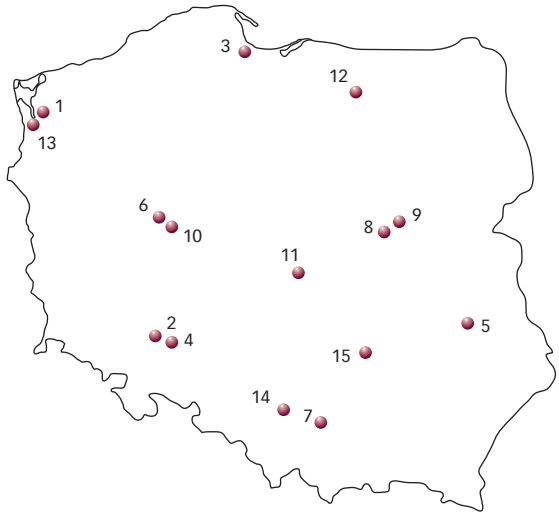

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Table 1: Patients Registered in HemoRec and in the Polish National Registry*

Diagnosis	Number of Patients Registered in HemoRec (% of all Diagnoses)	Number of Patients Registered in the National Registry (% of all Diagnoses)
Haemophilia A	834 (75.8)	2,213 (49.7)
Haemophilia B	134 (12.2)	387 (8.7)
Von Willebrand disease	54 (4.9)	1,187 (26.7)
Acquired haemophilia	35 (3.2)	34 (0.8)
Factor VII deficiency	29	193
Factor XI deficiency	1	33
Factor V deficiency	0	20
Factor X deficiency	1	15
Factor XIII deficiency	0	10
Factor XII deficiency	11	210
Fibrinogen defects	1	53
Rare clotting factor deficiencies – total	43 (3.9)	534 (12)
Platelet bleeding disorders	0	63
Vascular bleeding disorders	0	30
Other	0	5
Total number of diagnoses	1,100**	4,453
Diagnosis unknown	61	1
Total number of patients	1,110***	4,454

**Status as of 2 November 2010; **A total of 1,100 diagnoses were assigned to 1,049 patients of all 1,110 registered in HemoRec (44 patients had more than one diagnosis); ***In 61 patients the diagnosis was not specified.*

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