The Importance of Health Informatics in Public Health during a Pandemic
J. Mantas et al. (Eds.)

doi:10.3233/SHTI200532

Charting Early Developmental Trajectory of a Pilot Rare Disease Registry in Slovenia

Dalibor STANIMIROVIC [a,1], Eva MURKO [a],
Tadej BATTELINO [b,c] and Urh GROSELJ [b]
[a] *National Institute of Public Health, 1000 Ljubljana, Slovenia*
[b] *UMC - University Children's Hospital Ljubljana, 1000 Ljubljana, Slovenia*
[c] *University of Ljubljana, Faculty of Medicine, 1000 Ljubljana, Slovenia*

Abstract. Active surveillance of rare diseases enables evidence-informed policymaking, wide-ranging monitoring of rare disease patients, and subsequently assists progressively complex clinical and research needs. This article charts the initial steps for the development of a pilot rare disease registry in Slovenia. The research applies a case study design, while the collection of data was carried out through focus group discussions with 24 eminent experts from the field. The research results reveal the necessity for choosing an adequate development approach and point out that successful development of the national rare disease registry requires well-orchestrated efforts of all stakeholders. This inevitably includes effective preparation and implementation of the national rare disease policy, along with the divergence of clinical, organizational, and technological factors, and their integration with the long-standing public health goals.

Keywords. Rare diseases, pilot rare disease registry, case study, Slovenia

1. Introduction

In line with some indicative estimations, there are around 150,000 patients with rare diseases (RDs) in Slovenia [1]. Despite the lack of reliable epidemiological data, the abovementioned figures show that this area is of critical importance for the Slovenian healthcare system [2]. Deficient resources and knowledge in the field combined with the infrequency of RDs typically cause problems in their identification and diagnosis on one hand, while the chronicity and severity of RDs require complex and long-lasting clinical treatments on the other. Underdeveloped treatment approaches, which are often not supported by either relevant clinical evidence or appropriate medications, create additional difficulties. Insights into the problem reveal that information and communication technology (ICT) aspect in the field has been regrettably ignored, especially in terms of dedicated ICT solutions. In this context, RD registries are considered as essential tools for impartial monitoring of the prevalence and incidence of RDs, clinical studies, and can significantly assist patient treatment procedures [3]. Moreover, RD registries enable better assessment of clinical outcomes, and provide an

[1] Corresponding Author, Dalibor Stanimirovic, Centre for Healthcare Informatics, National Institute of Public Health, Trubarjeva Street 2, 1000 Ljubljana, Slovenia; E-mail: dalibor.stanimirovic@nijz.si.

applicable platform for evidence-informed policymaking. For that reason, the EU has declared the establishment of RD registries a priority in this field [4]. This is evidenced by several documents and projects [5, 6], and supported by the experience of countries that have already defined a framework for national registries and successfully implemented such initiatives [7-9]. However, despite the pressure from various national and international organizations, the Slovenian government only recently adopted the legislation requiring the mandatory establishment of the national RD registry. In view thereof, this article focuses on charting the initial steps for the development of the pilot RD registry (PRDR) in Slovenia.

2. Methods

The article applies a case study design to explore the research goals relating to the development of the PRDR in Slovenia. The collection of data was carried out through 14 focus group sessions conducted from January 2016 to February 2017.

Participants in the focus groups were selected according to their expertise and experience in the field of RDs [10]. A representativeness of the sample was ensured by a non-random stratified sampling approach. The final sample included 24 eminent experts coming from the most important institutions in the field of RDs. Conventional content analysis was used to assess the data obtained and provide the interpretation thereof, whereas the starting points for the development of the PRDR were extracted from the literature and focus group sessions.

3. Results

Planning the development of the PRDR was methodologically derived from the recommendations of the focus group participants and steps from the literature [11]:

The registry's purpose. The principal goals of the PRDR were focused on the different questions predominantly concerning the better quality treatment of the patients with RDs. Hence, the PRDR should generate reliable data regarding the incidence and prevalence, natural histories and diagnostic characteristics, and the management of RDs within the healthcare system.

Key stakeholders and the feasibility of the registry. The national project for the development of the PRDR was initiated by the leading institutions in the field related to clinical treatment of the RDs, public health, and healthcare informatics. Furthermore, registry team proposed certain regulatory amendments for the national RD registry, which were later actually introduced in the sectoral legislation.

Registry team. The team for the PRDR consisted of experts from clinical medicine, ICT/bioinformatics, genetics, and epidemiology, thus including all profiles, which are crucial for the successful development and implementation of the PRDR. The plan for actual operation of the PRDR (and forthcoming national RD registry) stipulated that registry team should contain administrative workers, health coders, and a supervisory body including patient representative.

Registry scope and data set. The PRDR should include all patients with a diagnosed RD and the pertinent OrphaCODE. The PRDR structure and suggested data set is displayed in Table 1. Patient demographic records containing personal data and vital status will be acquired from the Central Register of the Population, while the remaining

data would be provided by the reporting clinician. What is important, the data set for PRDR was adapted to ensure interoperability with the "Set of Common Data Elements for RD Registration" proposed by the European Commission's Joint Research Centre.

Table 1. Proposed data set for the Slovenian PRDR

Data set categories and their content
1. **Personal data:** UMCN; name/surname; gender; place of birth
2. **Vital status:** alive (Y/N); date and time of death
3. **Healthcare institution (of registration):** name; department; date of first contact; date of registration; name of clinician
4. **Diagnostic codes (main diagnosis)**: OrphaCODE; ICD-10 code
5. **Characteristics (main diagnosis):** description of the diagnosis; date of diagnosis; confirmed (Y/N); age at diagnosis; time of first signs/symptoms (year/antenatal/at birth/ND)
6. **Other diagnoses (all to be listed):** ICD-10 code; description
7. **Genetic characteristics and biological material**: HGNC code; HGVS code; OMIM number; type of biological material available; biobank name
8. **Functionality/Disability scores:** result according to the ICF classification
9. **Therapeutic data:** any orphan drugs (according to the EMA list)

List of abbreviations: EMA, European medicines agency; HGNC, The HUGO Gene Nomenclature Committee; HGVS, Human Genome Variation Society; ICD-10, International Classification of Diseases 10th Revision; ICF, international classification of functioning, diseases and health; N, no; ND, not determined; OMIM, Online Mendelian Inheritance in Man; UMCN, Unique Master Citizen Number; Y, yes.

Technological implementation. The activities for the design of technological solution were based on the recommendations of the focus groups and substantial outputs produced in each development step outlined above. The PRDR was constructed as a web application containing web-services, which significantly increase the functionality, simplify the use, and speed up the entire data entry/transfer process. The activities for the definition of clinical content and development of the technological solution were carried out separately. This concept allows experts to do the job as well as possible in their field; thus, clinicians can focus on defining clinical content, and ICT experts can focus on designing a technological solution. The national RD registry should have a central role in the future RD ecosystem, systematically connecting stakeholders and fragmented infrastructure, and providing required interoperability on all levels (technical, semantic, organizational, and legal). The designated institutions should form a well-organized reporting system, providing reliable data sources, standardized data formats, and high-quality data inputs for the national RD registry. Operations of the national RD registry will be conducted only in accordance with strict and predefined business rules. Compliance with the legal requirements, security policies, reporting procedures, and methodological standards should be regularly audited and prudently managed.

4. Discussion

The effective implementation of the RD registry requires a coordinated and systemic approach, along with the stakeholders' commitment, proficient political support and adequate sourcing [4]. This includes well-defined management framework, a viable ICT solution, and necessary resources (human, material, technical, and organizational) needed for its operation. Such approach should reduce the costs and workload of healthcare providers, and accelerate the acceptance of the RD registry among clinicians. The development the PRDR was indeed a very challenging project, as the entire process had to be carried out in a sensitive healthcare milieu, and all development steps were reliant on the regulatory, clinical, ICT, and other critical elements in the field of RDs.

The planned process for the development of the national RD registry will have to be grounded in feasible project plan that precisely defines the project leaders, funding, timeline, milestones, and long-term objectives. The proposed model for the development of the RD registry does not suggest a 'one-size-fits-all' solution; however, the presented study could offer some starting points for further advances in the field. Given the fact that Slovenia does not have a functioning national RD registry, all its implications were theorized without empirical validation in the real healthcare surroundings. Forthcoming research attempts should be focused on in-depth exploration of the role and effects of the national RD registry, including its evaluation in the actual clinical scenarios.

5. Conclusions

Notwithstanding the identified intricacies, the establishment of the national RD registry represents a considerable opportunity that may profoundly empower stakeholders, increase the exploitation of the current healthcare system capabilities, and facilitate the better-quality treatment of the patients with RDs. Owing to latest developments in the field, including the updated legislation and development of the PRDR, the general state of affairs relating to RDs in Slovenia seems reasonably optimistic.

Acknowledgements

The article was written within the project "Analysis and development of the rare diseases field in Slovenia", supported by the Slovenian Research Agency (1/10/2015 – 30/9/2017).

References

[1] Ministry of Health, Work plan in the field of rare diseases in the Republic of Slovenia, Ljubljana, Slovenia. Ministry of Health of the Republic of Slovenia, 2011.
[2] Valdez R, Ouyang L, Bolen J, Public health and rare diseases: oxymoron no more. Preventing chronic disease, 2016, 13:E05.
[3] Whicher D, Philbin S, Aronson N, An overview of the impact of rare disease characteristics on research methodology, Orphanet journal of rare diseases (2018), 13-14.
[4] National registries of rare diseases in Europe: an overview of the current situation and experiences, Public health genomics (2015), 18:20-25.
[5] European Union Committee of Experts on Rare Diseases – EUCERD. Recommendations on Rare Disease Patient Registration and Data Collection, Brussels, European Commission, 2013.
[6] EPIRARE project, European Platform for Rare Disease Registries. Specific objectives, Brussels, European Commission, 2011.
[7] Bellgard MI, Napier KR, Bittles AH, Szer J, Fletcher S, Zeps N, Goldblatt J, Design of a framework for the deployment of collaborative independent rare disease-centric registries: Gaucher disease registry model, Blood Cells, Molecules, and Diseases, (2018), 68:232-8.
[8] Nagel G, Ünal H, Rosenbohm A, Ludolph AC, Rothenbacher D, ALS Registry Study Group, Implementation of a population-based epidemiological rare disease registry: study protocol of the amyotrophic lateral sclerosis (ALS)-registry Swabia, BMC neurology 13(1) (2013), 22.
[9] Valent F, Deroma L, Moro A, Ciana G, Martina P, De Martin F, Bembi B, Value of the Rare Disease Registry of the Italian Region Friuli Venezia Giulia, Value in Health 22(9) (2019), 1003-11.
[10] Yin RK, Case study research and applications: Design and methods, Thousand Oaks, CA. Sage publications, 2017.
[11] Gliklich RE, Dreyer NA, Leavy MB, Registries for Evaluating Patient Outcomes: A User's Guide, 3rd ed. Rockville, MD. Agency for Healthcare Research and Quality, 2014.