

Original Article

Health Informatics Applications and Tourism: Personalized Information for Patients with Rare Diseases

Maria Mourtzou

National School of Public Administration and Local Government, Athens, Greece

Emmanouil Zoulias, MSc, PhD

Laboratory and Teaching Staff, School of Health Sciences, Faculty of Nursing, National and Kapodistrian University of Athens, Athens, Greece

Correspondence: Dr Emmanouil Zoulias, National and Kapodistrian University of Athens, School of Health Sciences, Faculty of Nursing, 123 Papadimitriou Str, 11527 Goudi, Athens, Greece, Email: ezoulias@nurs.uoa.gr

Work carried out: National School of Public Administration and Local Government, Athens, Greece

Abstract

Background: There is a research gap in this field, both in Greek and international literature. The purpose of this paper is to study the needs of patients with rare diseases, in particular as regards exploration and use of specialized tourism and therapeutic services, exploring at the same time the ways and perspectives of meeting these needs in Greece with the use of information and communication technologies.

Objective: This paper examines and discusses the role of health IT applications in terms of facilitating patients suffering from a rare disease, regarding needs or difficulties they face after diagnosis. This work focuses on the development of information technologies and tools that can meet the needs of patients with rare neuromuscular and neurodegenerative diseases when they wish to move to another place for tourism and/or therapeutic purposes.

Methodology: Methodologically, a systematic review of the literature was conducted through online databases.

Results: Rare diseases have a cumulatively high global impact. In addition to medical and pharmaceutical services, patients suffering from such diseases need complementary services that can improve their quality of life. Tourism and recreation, especially when combined with therapeutic intervention features such as rehabilitation and pain relief, can have multiple benefits for the quality of life of patients with rare diseases. The proposal of this work is the development of information technologies and tools of personalized information (web and mobile application), which can respond to the tourist and therapeutic needs of patients with rare diseases, providing information and guidance for access to specialized services.

Conclusions: The development of the applications, with consequent utilization of freely available data using interoperability, can bring significant benefits: to the quality of life of patients living with rare diseases and to the flourishing of a new health tourism sector in Greece.

Keywords: Mobile Applications, Web Applications, Health Tourism, Rare Diseases

Introduction

According to the definition of the European Union (EU), a disease is considered to be rare when it affects 1 in 2,000 people (ORPHANET, 2016), while, under the US institutional framework a disease is considered rare when it affects fewer than 200,000 people or about 1 in 1,500 (Congress, 2000). However, accumulatively, 6,000-8,000 rare diseases have been recorded which are estimated to affect around 27 to 37 million Europeans and 263 to

446 million people worldwide (National Organisation for Public Health, no date; Publications Office of the EU, no date; Nguengang Wakap *et al.*, 2020). Approximately 72% of rare diseases are of genetic origin and many of them are incurable and degenerative diseases that affect drastically patients' functionality and quality of life, often resulting in premature mortality (EURORDIS, no date). The average time for the correct diagnosis of a rare disease is at least 5-6 years from the onset of symptoms, while patients who suffer from a rare

disease and will never receive a diagnosis reach up to 50% (Nguengang Wakap *et al.*, 2020). The same difficulty is also encountered in the treatment of rare diseases, as most of them do not have medical treatment and thus patients' priority after diagnosis is the management of symptoms and the improvement of their quality of life. In this context, the contribution of special social services and complementary therapies, such as balneotherapy, thalassotherapy, etc., is highlighted. Even though there is no case in which the above can replace the appropriate medical treatment, they may act complementary, as part of a holistic and personalized care, providing a significant improvement in patients' quality of life.

Methodology

Methodologically, a systematic literature review was conducted. The search took place from July 2020 to September 2020, in the electronic portals and databases: Pubmed, Orphanet & Orphadata, Medscape, Elsevier, Taylor & Francis Online, SpringerLink, Google Scholar, as well as on the official websites of the European Organization for Rare Diseases (Eurordis) and the European Reference Networks for Rare Diseases .

Indicatively, the keywords used in various combinations for the research were: rare diseases, neuromuscular and neurodegenerative rare diseases, patient needs, social needs, information needs, priorities, travel with rare disease, adapted holidays, quality of life, symptom relief, rehabilitation, palliative care, balneotherapy, aqua therapy, curative tourism.

The inclusion and exclusion criteria from the review were:

(a) the studies to be relevant with the needs of patients with rare diseases, in particular neuromuscular and neurodegenerative diseases, (b) to focus on social needs and information needs, (c) to not concern diagnostic issues and medication or orphan drugs and (d) to have been published within the last fifteen years. Regarding the issue of therapeutic tourism, the inclusion criteria were its association with rare neuromuscular and neurodegenerative diseases and the publication within fifteen years.

Ethical considerations: A research ethical responsibility entails loyalty and honesty. This responsibility is realized in the selection of the object of study and methodology and during the handling of the data. General ethical principles and rules according to the World Medical Association Declaration of Helsinki (WMA)

from 2013, ICN (2012) and Etene (2001) are considered throughout.

Results

In total, more than 3,500 results were obtained from the searches in the above databases, with most of them concerning either the diagnosis or the pharmaceutical treatment of rare diseases, which is deducted from the inclusion criteria.

The studies meeting the basic inclusion criteria and evaluated as a full text were 78 and of these 14 were included in this review. The reasons for excluding the remaining studies are related to a lack of direct relevance to the specific objectives of this study. For example, several studies on the social and information needs of patients focused on education or employment issues, which are not targeted by this study.

Neuromuscular and neurodegenerative rare diseases: Rare neurological diseases are a broad group of disorders which affect the central and peripheral nervous systems and muscles. Overall they account for almost 50% of rare diseases (Federico, 2013). Particularly, Neurodegenerative, and neuromuscular rare diseases have several common symptoms, such as fatigue, muscle weakness, spasticity, dystonia, speech and movement disorders, pain, behavioral and sensory disorders, paralysis and premature mortality. Most of them are incurable diseases, where the appropriate management is multidisciplinary and supportive (European Reference Network – EURO-NMD, no date)(Matilla-Dueñas *et al.*, 2017) (Orphanet, 2013).

In that context, international literature points out the use of therapeutic tourism services (thermal springs, outdoor rehabilitation etc.) for diseases such as Motor Neuron Disease, Huntington's disease, Muscular Dystrophy etc. These services are used for exercise, empowerment, and rehabilitation purposes, helping significantly to reduce pain and thereby to reduce drug consumption, to ameliorate symptom management, to reduce fatigue and to improve functional mobility and spasticity. In the long term they contribute to the improvement of patients' life quality and mental health(Plecash and Leavitt, 2014; Atamturk and Atamturk, 2018; Lima and Cordeiro, 2020; Oluwatosin *et al.*, 2020; Rapolienè *et al.*, 2020).

Post-diagnostic patients' needs: Patients, after the diagnosis of a rare disease, often face difficulties covering their basic needs, such as the provision of specialized services and the access to

appropriate and valid information. Below, based on the systematic review of the literature, some basic needs of patients and their families which remain unfulfilled, are highlighted (table 1).

Table 1 Patients' Needs - Literature review

Needs / categories	Number of Patients	Percentage of patients with the need
Assistance in managing care coordination Or Coordinating service (care coordinator)	3.071	64% (81% among people with severe disabilities) (EURORDIS, 2017) ¹
	600	37% (Limb, Nutt and Sen, 2010) ¹
Information	3.071	70% (EURORDIS, 2017) ¹
	600	52% (Limb, Nutt and Sen, 2010) ¹
	68	100% (Litzkendorf et al., 2016) ²
Specialized rehabilitation services and related therapies	3.071	48% (EURORDIS, 2017) ¹
Customized holidays or therapeutic recreation	3.071	38% (EURORDIS, 2017) ¹
Adapted houses	3.071	30% (EURORDIS, 2017) ¹
Accessibility (in recreational activities etc.)	37	100% (Nierse et al., 2013) ³
Socialization	1.953	54% (EURORDIS, 2017) ¹
Social support	600	67% (Limb, Nutt and Sen, 2010) ¹
Psychological support	600	71% (Limb, Nutt and Sen, 2010) ¹
	3.071	47% (EURORDIS, 2017) ¹

Type of survey, 1 Quantitative, Questionnaire 2 Semi-structured interviews, 3 Interviews and focus groups

Discussion

Recently there is a global trend of promoting therapeutic/curative tourism as a tool to support patients with rare and chronic diseases. Therapeutic tourism reached a value of 678.5 billion dollars in 2017, with the relevant trips taking place annually accounting for 15% of the total trips, which puts him in the second place of tourist preferences after cultural tourism (Parisi and Papageorgiou, 2018). It includes the basic elements of a travel experience: transportation, accommodation, entertainment etc., in combination with therapeutic services: physiotherapy, rehabilitation activities in nature,

balneotherapies, thalassotherapies, etc. (Harahsheh et al., 2002; Parisi and Papageorgiou, 2018). Therapeutic tourism contributes to the relief of symptoms, the prevention of isolation often experienced by sufferers of a rare disease, the fulfilment of social needs and the improvement of life quality in the long term (Willson et al., 2018; Gül, 2019).

Greece's climate, natural and cultural environment, great coastline, and thermal springs make it an ideal location for the development of therapeutic tourism services for people with rare diseases. Especially the development of thermal therapy and thalassotherapy services, is regarded as a comparative advantage (Ministry of Tourism, 2018).

The country has a long history in terms of thermal springs. Since 1920 there has been a relevant institutional framework, Law 2188/1920, which defined the regulation for the operation of springs (Bakopoulou, 2010). Several legislative interventions followed, with the most significant being Law 3498/2006, which formed the institutional framework for the exploitation of thermal springs and the development of related infrastructures. That Law also established a General Register of Thermal Natural Resources (Government Gazette, 2006). Overall in Greece there are more than 750 hot springs (Danas, 2019), however, 70 of them are currently recognized (figure 1) (EOT, 2020).

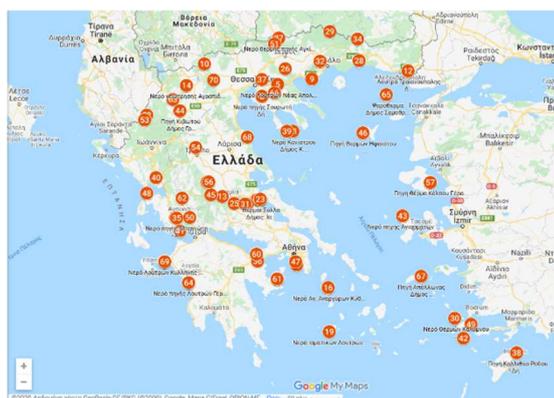


Figure 1. Recognized Therapeutic Natural Resources in Greece [28].

Despite the fact that Greece has a long history and dynamics in terms of wellness and thermal springs, it is not considered a destination for therapeutic tourism, as so far no targeted therapeutic infrastructures and activities have been developed (Nikoli, 2019). Thus, this option of complementary health care, which is ideal for

musculoskeletal and neurological disorders (Plecash and Leavitt, 2014; Oluwatosin *et al.*, 2020), remains neglected. In order for Greece to become a global destination for therapeutic tourism, investment incentives and funding programs for the creation of rehabilitation centers should be developed, along with sports activities, physiotherapy services, leisure activities and high-standard accommodation with increased accessibility (Bakopoulou, 2010; Parisi and Papageorgiou, 2018). In addition, the restructuring of this sector in our country and the exploitation of its potential requires a robust strategy, a concerted effort to cooperate between local-regional authorities and private enterprises and a dynamic marketing plan (Nikoli, 2019).

In order to connect the tourist and therapeutic services that Greece has with people suffering from rare diseases and their needs, the development of a personalized information application is proposed. It will consist of a web application to operate in computers and devices through web browsers, as well as an application for Android and iOS mobile devices (mobile application).

Through the applications users will be able to be informed about:

- The therapeutic services available in Greece (places-activities: thermal therapy, thalassotherapy centers, rehabilitation centers, etc.).
- The Centers of Expertise for Rare Diseases (places) available in Greece.
- The available hospitals and primary care units by region to which patients can turn in case of emergency (places).
- Points and activities of cultural interest in each region and details about their accessibility (places-activities).
- The recreational, sports and social activities that are organized in each area and their suitability according to each disease (activities).
- Accommodation and hotel units per area and details on their accessibility (places).

Here are some key features of the app, in its web and mobile version:

- Friendly design for people with special needs (WCAG standard).
- Design based on the rules and standards for the design and development of public administration websites.

- Open architecture (extensibility).
- Multilingualism.
- Web services and APIs, for the utilization of systems interoperability.
- Navigation supported by Google Maps and GPS.
- Regular updating of information.
- Optional login and user profile creation to collect data and provide personalized suggestions.
- Integration of an in-app tool to investigate users' needs in order to gather data for future research and further expansion of the application.

Data: Keystone of the applications are the data concerning rare diseases and their symptoms. These data will be drawn from the European portal for rare diseases “Orphanet”. Access is provided through the Orphadata website. The data are freely available in XML file format under the terms of the “Commons Attribution 4.0 International (CC BY 4.0)” license. The translation and adaptation of Orphanet data may be carried out by a competent national team following the signing of a data transfer agreement with the Orphanet Coordination Group (Orphanet, 2017).

The Orphanet nomenclature is organized into a multi-hierarchical classification and each disease has a unique and stable identifier, the ORPHA code. There is, however, alignment with the World Health Organization’s (WHO) International Classification of Diseases (ICD) and full alignment with the new ICD-11 standard, which is more complete in the inclusion of rare diseases, is expected soon (Aymé, Bellet and Rath, 2015). This is particularly important for the development of the proposed applications, as the ICD standard is the most widespread in Greece, and thus the adoption of ICD-11 will help to facilitate interoperability between national information systems.

Interoperability: The interoperability of the web or mobile application with other information systems, as well as the connection between data on rare diseases encoded in ICD-11, points of interest (places) and services/activities, are particularly important issues.

The following table briefly illustrates the interoperability of the applications.

Table 2. Web & mobile application interoperability

Proposed web and mobile app	Data about rare diseases and their symptoms ((ICD-11)
Culture and Sports Ministry and Official websites of Municipalities (or thermal springs websites of each region)	Data on cultural points of interest and cultural or sporting activities in each region. Places & activities.
Ministry of Health and Health Atlas	Data on the existing structures and health services (e.g. hospitals, rehabilitation centers, centers of expertise). Places.
Ministry of Tourism and Hellenic Chamber of Hotels	Data on the available tourism facilities and accommodation, as well as their accessibility. Places.
Association of Municipalities and Communities of Thermal Springs in Greece	Data on the available therapeutic structures and services (e.g. thermal treatment centers). Places & activities.

SWOT Analysis

Below is a brief SWOT Analysis approach on the development of therapeutic tourism for patients with rare diseases in Greece, through the creation of the proposed applications. It becomes evident that while there are weaknesses and external threats to be addressed, strengths and opportunities are particularly important. Indeed, given that some of the weaknesses could be addressed by exploiting the opportunities in the external environment (e.g. research gap-research programs, restructuring costs-funding programs), the implementation of such a project seems to have a positive outlook for Greece.

Internal environment

Strengths

- Existence of basic infrastructure and natural resources.
- Greece is already an entrenched tourist destination.
- Meeting different therapeutic needs (diversity of services).
- It can generate significant government revenues and economic benefits.
- It contributes to the diversification of the tourism product, which is a long-term goal of the country.
- Exploitation of existing know-how and

technological resources of the public sector.

- Important supporting factors, such as the climate and cultural wealth of the country.

Weaknesses

- Additional research and data are required
- A comprehensive needs investigation for all rare diseases is required in order to avoid exclusions in patient categories.
- Restructuring existing infrastructure and creating new ones that meet patients' needs is a time-consuming and costly process.
- Strengthening of local competencies and initiatives, as well as institutional changes are required.

External environment

Opportunities

- There is a research and market gap regarding this project.
- It presents utility for millions of people worldwide.
- There are research and business funding programmes for innovative ideas on rare diseases, such as the European "E-Rare"¹.

Threats

- Financial difficulties and lack of investment interest.
- Electronic illiteracy and non-use of new technologies by a large audience category.
- Climate change could threaten the country's natural resources and infrastructure.
- Competition developing from neighboring countries and other countries within the EU in the therapeutic tourism sector.

Conclusion

The population affected by a rare disease worldwide amounts to 263 to 446 million people [3]. Most rare diseases are incurable and degenerative, which demonstrates, in addition to the medical and pharmaceutical need for progress, the usefulness of complementary services that can contribute to better symptom management and improvement of patients' life. Therapeutic tourism can have significant benefits to the holistic management of a rare disease and to the patients' quality of life.

Taking into account the post-diagnostic needs of the patients, as well as the positive prospects of Greece as a destination for therapeutic tourism, it is proposed to create a personalized information application (web & mobile edition) for patients

¹ <http://www.erare.eu/project>

with rare diseases, through which they will be able to plan a therapeutic tourism trip in our country that responds to their needs. The applications will utilize freely available data through interoperability and development of Web technologies and APIs. As this is a relatively uncharted field, the applications will also integrate a tool for further investigation of users' needs, in order to gather data for future research.

The research interest that has emerged recently for rare diseases mainly concerns their diagnosis and the development of medication, while therapeutic tourism is also a new sector of health tourism. Their robust and well-documented connection requires extensive research, especially in terms of patients' needs and expectations of a therapeutic tourism trip. The proposed information technology tools aim to contribute precisely in this direction, as, on the one hand they facilitate the development of the therapeutic tourism sector in our country and the access of people with rare diseases to specialized services, and on the other hand they contribute to further exploration of patients' needs and to the encouragement of future research. However, further primary research and collaborations with universities, research institutes and European programs are considered crucial in this field.

References

- Atamturk, H. and Atamturk, A. (2018) 'Therapeutic effects of aquatic exercises on a boy with Duchenne muscular dystrophy', *Journal of Exercise Rehabilitation*. Korean Society of Exercise Rehabilitation, 14(5), pp. 877–882.
- Aymé, S., Bellet, B. and Rath, A. (2015) 'Rare diseases in ICD11: Making rare diseases visible in health information systems through appropriate coding', *Orphanet Journal of Rare Diseases*. BioMed Central Ltd., 10(1), pp. 1–14.
- Bakopoulou, R. (2010) *Prospects for the Development of Spa Tourism in Greece: Comparisons with European Experience and Practice*. Available at: https://www.ekdd.gr/ekdda/files/ergasies_esdd/20/025/1402.pdf.
- Congress, U. (2000) *RARE DISEASES ACT OF 2002*.
- Danas, M. (2019) *Development Strategy of Thermal Springs in Greece*. Athens: Association of Municipalities of Thermal Springs of Greece.
- EOT (2020) *Complete Register of Recognized Thermal Natural Resources on the website of the ministry*. Athens. Available at: <http://www.gnto.gr/el/22012020-complete-register-recognized-iamatical-natural-resources-on-the-page-of-the-ministry>.
- European Reference Network – EURO-NMD (no date) *ERN-EURO-NMD: Diseases Covered*. Available at: <https://ern-euro-nmd.eu/disease-covered/> (Accessed: 2 March 2021).
- EURORDIS (2017) *Juggling care and daily life*. Available at: http://download2.eurordis.org.s3.amazonaws.com/rbv/2017_05_09_Social_survey_leaflet_final.pdf (Accessed: 2 March 2021).
- EURORDIS (no date) *What is a rare disease?* Available at: <https://www.eurordis.org/content/what-rare-disease> (Accessed: 2 March 2021).
- Federico, A. (2013) 'Rare neurological diseases: A Pandora's box for neurology (an European and Italian perspective)', *Revue Neurologique*. Elsevier Masson, 169(SUPPL.1), pp. S12–S17.
- Government Gazette (2006) *Law number 3498: Development of spa tourism and other provisions (Government Gazette AD 230 / 24.10.2006)*. Available at: <https://www.e-nomothesia.gr/kat-tourismos/n-3498-2006.html>.
- Gül, S. (2019) 'Palliative care tourism (PCT) as one new focus for medical tourism', in *Research & Reviews in Social, Human and Administrative Sciences*. Ankara - Gece Akademi.
- Harahsheh, S. S. (2002) *Curative Tourism in Jordan and its Potential Development Thesis for the fulfillment of MA in European Tourism Management (ETM)*.
- Lima, A. A. R. de and Cordeiro, L. (2020). Aquatic physiotherapy in individuals with muscular dystrophy: a systematic scoping review', *Physiotherapy and Research*. FapUNIFESP (SciELO), 27(1), 100–111.
- Limb, L., Nutt, S. and Sen, A. (2010) 'Experiences of rare diseases: an insight from patients and families', *Rare Disease*.UK
- Litzkendorf, S. Babac1 A, Rosenfel D, Franziska Schauer F, Hartz T, Luhrs V, J Graf von der Schulenburg M, and Frank M. (2016) *Information Needs of People with Rare Diseases-What Information Do Patients and their Relatives Require?* *Journal of Rare Disorders: Diagnosis & Therapy*, 2, 2, 40. This article is available from: <http://raredisorders.imedpub.com/archive.php>
- Matilla-Dueñas A, Corral-Juan M, Rodríguez-Palmero Seuma A, Vilas D, Ispierto L, Morais S, Sequeiros J, Alonso I, Volpini V, Serrano-Munuera C, Pintos-Morell G, Álvarez R, Sánchez I. (2017). Rare Neurodegenerative Diseases: Clinical and Genetic Update. *Adv Exp Med Biol*. 1031:443-496.
- Ministry of Tourism (2018) *Draft Law: "Thematic tourism - Special forms of tourism - Arrangements for the modernization of the institutional framework in the field of tourism and tourism education - Support for tourism entrepreneurship and other provisions*. Available at: <http://www.opengov.gr/tourism/wp->

- content/uploads/downloads/2018/06/s_n_themati kos_tourismos.pdf (Accessed: 2 March 2021).
- National Organisation for Public Health (no date) *Dare Disease*. Available at: <https://eody.gov.gr/disease/spania-nosimata/> (Accessed: 2 March 2021).
- Nguengang Wakap, S. Lambert D.M. Olryl A. Rodwelll C. Gueydan C. Lanneau V. Murphy D. Le Cam Y, Rath A., (2020) 'Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database', *European Journal of Human Genetics*. Springer Nature, 28(2), 165–173.
- Nierse CJ, Abma TA, Horemans AM, van Engelen BG. (2013). Research priorities of patients with neuromuscular disease. *Disabil Rehabil*. ;35(5):405-12.
- Nikoli, G. (2019) *Georgia Nikoli / Athina Lazakidou A review of thermal tourism in Europe and Greece, Tourism: An International Interdisciplinary Journal*. Institut za turizam.
- Oluwaseun O.T., Makama A.Y., Ibrahim S.Z., Rahman S. A., Oladimeji O. (2020) Balneotherapy/Spa Therapy: Potential Of Nigerian Thermal Hot Spring Waters For Musculoskeletal Disorders And Chronic Health Conditions'. 'International Journal of Advanced Research and Publications, 4,3, 95-100, Available at: www.ijarp.org (Accessed: 2 March 2021).
- Orphanet (2013) *Krabbe disease*. Available at: [https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=22&Disease_Disease_Search_diseaseGroup=Krabbe&Disease_Disease_Search_diseaseType=Pat&Disease\(s\)/group_of_diseases=Krabbe-disease&title=Krabbe-disease&search=Disease_Search_Simple](https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=22&Disease_Disease_Search_diseaseGroup=Krabbe&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group_of_diseases=Krabbe-disease&title=Krabbe-disease&search=Disease_Search_Simple) (Accessed: 2 March 2021).
- Orphanet (2017) *Procedural document: Orphanet Rare Diseases Nomenclature Production in National Language Procedural document on Orphanet Rare Diseases Nomenclature Production in National Language*. Available at: [www.orphadata.orghttp://www.orpha.net/orphacom/cahiers/docs/GB/eproc_Nomenclature-production-National-language.pdf](http://www.orpha.net/orphacom/cahiers/docs/GB/eproc_Nomenclature-production-National-language.pdf). (Accessed: 2 March 2021).
- ORPHANET (2016) *About rare diseases, About Rare Diseases*. Available at: https://www.orpha.net/consor/cgi-bin/Education_AboutRareDiseases.php?lng=EN (Accessed: 2 March 2021).
- Parisi, E. and Papageorgiou, A. (2018) 'Wellness tourism: an attractive alternative tourism form', in *TOURMAN 2018 Conference Proceedings*. Rhodes.
- Pleash, A. R. and Leavitt, B. R. (2014) 'Aquatherapy for neurodegenerative disorders', *Journal of Huntington's Disease*, pp. 5–11.
- Publications Office of the EU (no date) *Rare diseases*. Available at: <https://op.europa.eu/en/publication-detail/-/publication/c2ba4fd4-ae31-11e7-837e-01aa75ed71a1> (Accessed: 2 March 2021).
- Rapolienė L, Razbadauskas A, Mockevičienė D, Varžaitytė L, Skarbalienė A.(2020).. Balneotherapy for musculoskeletal pain: does the mineral content matter? *Int J Biometeorol*; 64(6):965-979.
- Willson, G. McIntosh A.G., Morgan A. Sanders D. (2018) 'Terminal illness and tourism: a review of current literature and directions for future research', *Tourism Recreation Research*., 43(2), pp. 268–272.