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# Improving the visibility of Rare Diseases in General Medical Practice

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**Abstract**

Rare diseases (RDs) are individually rare but collectively common, affecting 1 in 17 people globally. Many RDs are complex and multi-systemic and are represented in all medical specialities. Lack of information and awareness of RDs often leads to people living with RDs experiencing a long and difficult diagnostic journey, the 'diagnostic odyssey', with delayed access to appropriate treatment. Here we highlight some of the validated web-based sources of RD information and expertise that can be used by general physicians in hospitals and the community to support people living with a RD and assist with rare disease patient referrals. The resources described include: European RD strategies; the RD European Reference Networks (ERNs), the European RD portal Orphanet; RD coding using ORPHAcode; RD Communities and RD Global Platforms; the RD Patient Voice and RD patient organisation alliances; and the National Rare Diseases Office.

## Background

A Rare Disease (RD) is defined in Europe as a disease that affects less than 5 in 10,000 (1 in 2,000) people. RDs are a global public health priority with unmet healthcare needs and are included in the UN Sustainable Development Goals and the UN Resolution on Addressing the Challenges of Persons Living with a Rare Disease [1, 2]. There are currently over 6,000 RDs, more than 5,000 of which are ultra-rare (prevalence of less than 1 person per 100,000) [3]. Although individually rare, collectively RDs are common with an estimated 1 in 17 people globally living with a RD. The challenges faced by people living with a rare disease (PLWRD) and the healthcare professionals caring for them are the prolonged and difficult diagnostic journey ('diagnostic odyssey'), the lack of information on RDs and lack of awareness of RDs in the community. There are many people known to have an as-yet undiagnosed RD or a syndrome without a name (SWAN) [4]. Without an accurate diagnosis, the affected individual often cannot access the necessary services and supports. A high percentage of RDs have a genetic origin (72%), which has implications for relatives and family planning. Many RDs are complex and multi-systemic, requiring specialised care, and PLWRD use a disproportionate amount of health service resources [3]. It is difficult for any individual or country to have the expertise and knowledge to treat all RDs [5]. This is exacerbated by a lack of clinical practice guidelines (CPGs) for RDs, and care pathways to enable referral for diagnosis and treatment [6]. Expanded knowledge regarding diagnosing and managing RDs is highly relevant for all healthcare professionals, specialists and general

practitioners [7]. A recent European (Eurordis) Rare Barometer study has indicated that the average total diagnosis time for PLWRD in Europe approached five years [8].

*European RD Strategy*

Since the Council of the European Union, made Recommendations in 2009 on an action in the field of rare diseases the EU has continued to expand and consolidate strategic action to improve RD patient access to diagnosis, information and care [9]. To enhance access to RD expertise across Europe, the 2011 Cross Border Care Directive (2011/24/EU) and 24 European Reference networks (ERNs) were established covering the range of medical specialties to enable patients, health care professionals and researchers to access specialist RD knowledge and expertise without the need to travel [10]. Requests can be made to ERN coordinators by RD clinical experts at centres of expertise linked to ERNs to convene a virtual (using dedicated IT platforms) advisory panel of clinical experts from relevant medical specialties across Europe to review a patient's diagnosis and treatment. The ERNs provide RD information and education for patients and health professionals.

*Orphanet*

The Orphanet European RD portal was established in 1997 in France as a reference source of information on RDs and has gradually expanded its function with EU support. Orphanet provides free access to high-quality scientific information on RDs that is expert-validated and continuously updated, and a directory of expert services by disease: centres of expertise, laboratories and diagnostic tests, patient organisations, research projects, clinical trials, and clinical practice guidelines. This facilitates access to RD expertise and knowledge [11].

*RD Coding (ORPHAcodes).*

Orphanet provides a common language by developing and maintaining a unique, multi-lingual nomenclature of RDs (ORPHAcodes) that is aligned with other terminologies: OMIM, ICD, SNOMED-CT, MedDRA, UMLS, MeSH, and GARD. The Orphanet nomenclature enables interoperability of healthcare databases and increased visibility of RDs in healthcare information systems [11]. Recently, the 'RD-CODE' project released official guidelines for using a new ORPHAcode for Undiagnosed RD Patients (ORPHA:616874), which aims to improve the diagnostic pathway for undiagnosed RDs [9].

*RD Communities and RD Global Platforms*

Ongoing advancements in precision medicine have driven a need for moderated global online platforms where PLWRDs and their families can connect, share experiences, and source best practice information [10]. The international group 'Unique' has facilitated a global network of families living with rare chromosome disorders and autosomal single-gene disorders. This network has enabled the development of hundreds of specialist information guides and booklets for patients and health professionals and increased understanding and awareness of these disorders [14]. The US-based

international research programme, '*Simons Searchlight*', has developed a natural history database, biorepository, and resource network of over 175 rare genetic neurodevelopmental disorders to advance the understanding of these conditions [15]. The National Institutes of Health's, Genetic and Rare Diseases Information Center (*GARD*) and the National Organization for Rare Disorders (*NORD*) in the US provide free access to reliable, easy-to-understand information about genetic and rare diseases [16,17].

*RD Patient Voice*

In the area of RDs, the patient voice and expertise are particularly important to provide experience and patient-reported outcomes. *EURORDIS* – Rare Diseases Europe, is a unique, non-profit alliance of over 1000 rare disease patient organisations from 74 countries working together to strengthen the RD patient voice and shape research, policies, and patient services to improve the lives of PLWRDs [18]. *NORD* is a coalition of patients and caregivers representing a unified voice for all Americans with RDs [17]. Rare Diseases Ireland (*RDI)* is a national alliance of RD patient organisations working to improve the lives of the estimated 300,000 PLWRDs in Ireland [19].

*The Irish National Rare Diseases Office (NRDO)*

The NRDO is the national rare disease 'coordination hub' for the Republic of Ireland [20]. This was established in 2015 as a key recommendation of the first National Rare Diseases Plan for Ireland. The NRDO aims to support PLWRDs, their families and healthcare professionals. It provides evidence-based RD information through the National RD Information Line (telephone and email contact); hosts and curates Orphanet Ireland; supports integration of national RD centres of expertise and European Reference Networks into the national health care system; and provides RD education and training. Our combined user experience has illustrated the utility of signposting to the appropriate centres of expertise, and the provision of reliable information to PLWRDs and their families, improving the diagnostic and care journey. See Figure 1 for case examples.

There are numerous approaches to address the unmet needs of PLWRDs and their families. This report highlights the utility of web-based resources that general physicians can use to assist with RD patient referrals, and the value of a national information office to improve the experience of PLWRDs.

**Declarations of Conflicts of Interest:**

Aileen Timmons, Darragh Nerney and Eileen Treacy are part of the Orphanet Ireland team.

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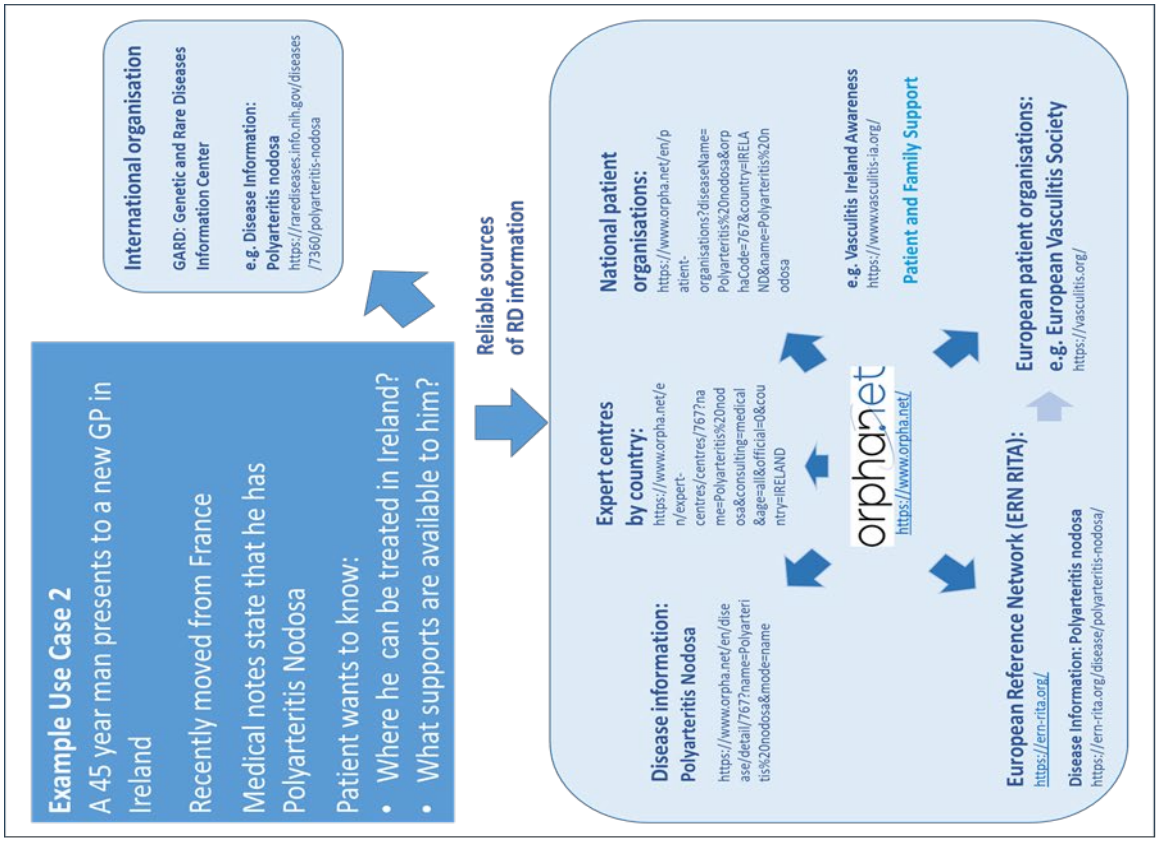


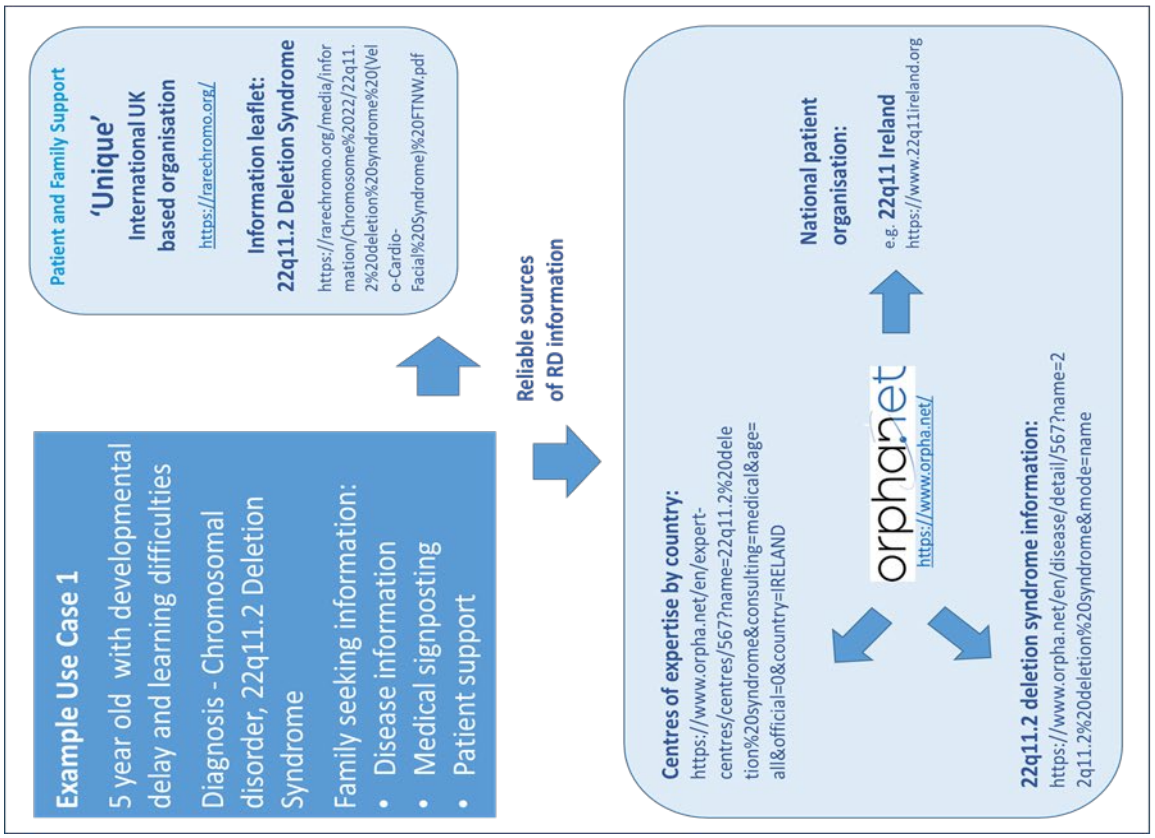


**Figure 1:** Example use cases demonstrating the utility of a national rare diseases Information service and web-based resources to support people living with a rare disease and relevant health care professionals.

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