VALUE IN HEALTH 21 (2018) 491–492

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

THEMED SECTION: RARE DISEASES

Editorial

Rare Diseases: Addressing the Challenges in Diagnosis, Drug Approval, and Patient Access

Rare diseases represent a wide range of disorders and constellations of clinical signs and symptoms. Many rare diseases cause chronic or progressive physical deterioration, disability, or premature death and start in childhood, creating a huge burden on parents and caregivers. Most rare diseases are thought to be genetic and there may be as many as 7000 rare diseases [1]. Although there is no universally accepted terminology or definition as to what constitutes a rare disease, it is typically characterized by its low frequency of occurrence. A global review of rare disease terminology found that 58% of definitions included a prevalence threshold with an average global threshold of 40 cases per 100,000 people [2]. Although the frequency of a single rare disease is low, because of the large number of rare diseases, the total number of people with a rare disease is large.

Rare diseases became known as orphan diseases because drug companies were not interested in adopting them to develop treatments. The Orphan Drug Act of 1983 passed by the US Congress created incentives to encourage companies to develop new drugs for rare diseases. There is similar legislation in the European Union. Drugs are granted an orphan designation if they are for the treatment of rare diseases that are life-threatening or seriously debilitating. The definition of "rare disease" varies from jurisdiction to jurisdiction, being a disease or condition affecting fewer than 200,000 patients in the United States (6.4 per 10,000 inhabitants), or a disease with a prevalence of 5 per 10,000 inhabitants or lower in the European Union [3]. In the decade leading up to the passage of the Orphan Drug Act, only 10 industry-supported products for rare diseases were brought to market. Since 1983, more than 600 orphan drug indications were approved from more than 450 distinct drug products, representing a huge increase in rare disease research and clinical development of new technologies [4].

Nevertheless, the development of new rare disease therapies has encountered significant obstacles with respect to understanding the incidence and prevalence (epidemiology), patient-reported burden of disease, economic cost of the disease and treatment, health technology assessment, and patient access. In June 2013, two working groups were established by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) under the ISPOR Rare Disease Special Interest Group. An article by the first working group provided rare disease terms and definitions [2]. The second working group (Challenges in Assessment and Appraisal of Diagnostics and Treatments Working Group) undertook a broad identification of challenges confronting those engaged in rare disease–focused research and development, as well as technology assessment.

Subsequently, *Value in Health* issued a special Call for Papers to attract submissions for a themed section dedicated to rare diseases. The resulting nine selected articles are published in this issue.

1. The first article, written by a group of authors from the ISPOR Rare Disease Special Interest Group, develops a multistakeholder catalogue of the principal difficulties faced in real-life rare disease research [5].
2. The article by Auvin et al. [6] provides a method to estimate the prevalence of rare diseases on the basis of reported incidence, to capture the time it takes for the diagnosis of newly discovered rare diseases to become part of mainstream diagnostic practice.
3. Building on a previously published report in *Value in Health* titled "Patient-Reported Outcome and Observer-Reported Outcomes Assessment in Rare Disease Clinical Trials: An ISPOR Clinical Outcome Assessment Emerging Good Practices Task Force Report" [7], the article by Phillips [8] in this issue describes rare disease clinical outcome assessments specific to pediatric patients and developmental changes while maturing.
4. The article by Knight et al. [9] describes economic modeling considerations for rare diseases and strategies that manufacturers have used to overcome challenges in submissions to the highly specialized technologies of the National Institute for Health and Care Excellence in England and in ultra-orphan appraisals to the Scottish Medicines Consortium.
5. Schlander et al. [10] conducted a systematic review of the literature-reported expenditures for drugs for rare and ultra-rare diseases in Europe to explore the budget impact of rare diseases.
6. The article by Magalhaes [11] reports a structured deliberation to elicit and describe the values of the general public in Alberta, Canada, regarding whether the severity of a rare condition can achieve priority in funding over common conditions, and what aspects of a condition drive this judgment.
7. The article by Hughes et al. [12] reports a person trade-off and discrete choice experiment among 3950 adults representative of the UK general population to estimate societal preferences for funding of non–cost-effective orphan drug treatments (i.e., Does the UK general public consider rarity in itself as being sufficient to justify special consideration for additional National Health Service funding?).
8. The article by Ollendorf et al. [13] explores the general ethical dilemmas that rare diseases present, the rare disease landscape in health technology assessment and US payer systems, the role of contextual factors in rare diseases (beyond cost effectiveness), and possible ways forward.
9. The final article by Kos et al. [14] investigates patient access to medicines for rare diseases from the Orphanet list in various European countries in the past decade using IMS Health sales data.

Although the international community has taken steps to address the rare disease challenges outlined in these articles, it has done so with a high degree of variation. The ISPOR Rare Disease Special Interest Group plans to continue its multi-stakeholder efforts toward providing recommendations to address rare disease challenges regarding evidence generation and health technology assessment. This collection of articles should help those attempting to address these challenges.

Kati Copley-Merriman, MS, MBA
RTI Health Solutions
Ann Arbor
MI, USA

1098-3015/$36.00 – see front matter Copyright © 2018, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

https://doi.org/10.1016/j.jval.2018.03.009

REFERENCES

[1] National Institutes of Health. Available from: http://rarediseases.info.nih.gov. [Accessed March 13, 2018].
[2] Richter T, Nestler-Parr S, Babela R, et al. Rare disease terminology and definitions—a systematic global review: report of the ISPOR Rare Disease Special Interest Group. Value Health 2015;18:906–14.
[3] Franco P. Orphan drugs: the regulatory environment. Drug Discov Today 2013;18:163–72.
[4] Lanthier M. Insights into rare disease drug approvals: trends and recent developments. Available from: http://www.fda.gov/downloads/ForIndustry/DevelopingProductsforRareDiseasesConditions/UCM581335.pdf. [Accessed March 13, 2018].
[5] Nestler-Parr S, Korchagina D, Toumi M, et al. Challenges in research and health technology assessment of rare disease technologies: report of the ISPOR Rare Disease Special Interest Group. Value Health 2018;21:493–500.
[6] Auvin S, Irwin J, Abi-Aad P, Battersby A. The problem of rarity: estimation of prevalence in rare disease. Value Health 2018;21:501–7.
[7] Benjamin K, Vernon MK, Patrick DL, et al. Patient-reported outcome and observer-reported outcome assessment in rare disease clinical trials: an ISPOR COA Emerging Good Practices Task Force Report. Value Health 2017;20:838–55.
[8] Phillips D. Clinical outcome assessments: use of normative data in a pediatric rare disease. Value Health 2018;21:508–14.
[9] Pearson I, Rothwell B, Olaye A, Knight C. Economic modelling considerations for rare diseases. Value Health 2018;21:515–24.
[10] Schlander M, Dintsios CM, Gandjour A. Budgetary impact and cost drivers of drugs for rare and ultra-rare diseases. Value Health 2018;21:525–31.
[11] Magalhaes M. Can severity outweigh smaller numbers? A deliberative perspective from Canada. Value Health. 2018;21:532–7.
[12] Bourke S, Plumpton C, Hughes DA. Societal preferences for funding orphan drugs in the United Kingdom: an application of person trade off and discrete choice experiment methods. Value Health 2018;21:538–46.
[13] Ollendorf D, Chapman R, Pearson SD. Evaluating and valuing drugs for rare conditions: no easy answers. Value Health 2018;21:547–52.
[14] Deticek A, Locatelli I, Kos M. Patient access to medicines for rare diseases in European countries. Value Health 2018;21:553–60.