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Patient's forum

The role of patient advocacy organisations in neuromuscular disease R&D – The case of the Dutch neuromuscular disease association VSN

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ABSTRACT

This article investigates to what extent patient advocacy organisations play a role in influencing R&D and policymaking for rare neuromuscular diseases. The Dutch neuromuscular disease organisation VSN is studied in depth. A brief history of the VSN is sketched along with the international embedding of the organisation. Then, a more general perspective is provided on the reasons and extent of the involvement of patient organisations (and especially the VSN) in innovation processes. Lastly, internal mechanisms are presented that can best be applied by these organisations. The VSN adheres to a rare, long-term vision on drug innovation that requires long-term planning and policy and vision creation and steering the direction of science and technology. At the same time, other actors like scientific organisations and science policymakers and managers can benefit from these lessons to learn how to deal with patients and patient organisations in the future.

1. Introduction

Neuromuscular diseases are a heterogeneous group of life-threatening or chronically-debilitating conditions. None of these diseases have a prevalence above 5 out of 10,000 inhabitants of the European union. As such, they are examples of so-called rare diseases. These ailments are subject to huge challenges: despite the urgent health needs of persons with rare diseases, drugs for these diseases are known as 'orphans' because companies and scientists are not eager to 'adopt' them. The small amount of patients does not offer enough potential for economic profitability or scientific prestige.

Of course these perspectives are too shallow and black-and-white. Not in the least because companies, like Genzyme and Shire, proved that orphan drugs can be the basis of a viable business model, and a large range of scientists keep emphasising that research on rare diseases can function as a scientific model system for other, more prevalent diseases [1].

In the light of these challenges and opportunities, a wide range of actors continue to stress the importance of investing in rare diseases [2,3]. Especially two public initiatives form prominent examples of this emphasis. Firstly, the Orphan Drug Act in the US (since 1983) and the EU Orphan Drug Regulation (since 2000) were decreed, in the context of which medicines can obtain an Orphan Drug Designation that guarantees, amongst other incentives, market exclusivity and protocol assistance. Secondly, a WHO/EU project called 'Priority medicines for Europe and the world' aimed to construct, in consultation with scientists, industry and patient groups, a list of diseases that should be the cornerstone of public investment in drug R&D [4]. Drugs for rare diseases were designated as a priority in this report.

Despite these initiatives, rare neuromuscular diseases inherently imply a small basis for support. The stakeholders with the strongest incentives to stimulate R&D are patients. Therefore, some authors claim that patients and their representative organisations more actively stimulate and steer others to work on R&D in comparison with patients (organisations) focussing on more common diseases [5,6]. These organisations should take the lead in these disease areas because other players would be less willing to do so. For example, patient organisations can serve as "lubricating oil in the difficult relationship between industry and science" [7].

This article investigates to what extent patient advocacy organisations play a role in influencing R&D and policymaking for rare neuromuscular diseases, and if so, what kind of internal mechanisms can best be applied by these organisations. These insights can be helpful for patient organisations to optimise stimulating and steering neuromuscular disease R&D. Moreover, it might increase the understanding of other stakeholders, such as scientific and medical professional groups and businesses, as to how to benefit from patient involvement. Lastly, concerning the scientific relevance, we build on literature about patient advocacy groups [8,9], which has mushroomed from the 1990s onwards [10].

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A prominent Dutch example that is presented here is the Dutch neuromuscular disease organisation (Vereniging Spierziekten Nederland, VSN).

This historical report proposes to follow the VSN's efforts in neuromuscular disease research, by studying the activities, documents, statements of the patient organisation and the actors with which it has interacted over these 40 years. This is based on a study done by Boon [6]. The topics that were taken into account were amongst others biomedical research, diagnostics, innovative therapies, and patient registries.

2. History of the VSN and its related international networks

The Dutch Neuromuscular disease organisation is a patient organisation founded in 1967 by two parents with children who suffered from a neuromuscular disease. Objectives included taking care of the welfare of and communication to patients and parents, setting-up mutual help groups for different neuromuscular diseases, and stimulating research into neuromuscular diseases.

The VSN soon put research that would improve the diagnosis of neuromuscular diseases on their agenda. To this effect, the patient organisation established contact with several medical professionals, scientists, and charity funds. Under the adage that scientists working on rare diseases needed to share their work to be effective, the VSN co-founded the European alliance of neuromuscular disorders associations (EAMDA) in 1971. EAMDA's objectives included coordinating and stimulating international research, and setting-up comparative quantitative data inventories on therapy, diagnostics, research, and prevalence. For example, a 1984 international workshop on Duchenne muscular dystrophy resulted in a coordinated research effort that led to finding the gene responsible for the disease. This also marked the start of the VSN's interest into translating this genetic information into diagnostics and therapy, amongst others by stimulating the set-up of patient registries.

In the 1980s two other science collaborations were co-founded by the VSN: the Dutch Foundation for Neuromuscular Research (SONMZ; 1985) together with doctors and researchers, and the European Neuromuscular Centre (ENMC; 1988) together with other patient organisations, such as the Association Française contre les Myopathies. The ENMC stimulated international research, notably through the organisation of scientific workshops, an information gateway, and a clinical trial network. To date nearly 2000 scientists have taken part in more than 160 workshops. Issues that were discussed during these workshops included criteria for diagnostics, standardising clinical trials, and gene location [11,12]. The effectiveness of these workshops is underlined by the fact that workshop reports are amongst the most cited articles in NMD. The workshops now embrace wider issues around patients' lives and well-being as well. A programme of practical care workshops, which will run alongside the science workshops, is planned.

In 1998, the VSN reflected on its research steering and stimulating role, and widened its attention to include therapy. One of the diseases for which this was topical at that time was Pompe disease. Once again the VSN thought that this could best be done on an international level and it initiated the International Pompe Association.

In the 2000s the VSN widened their perspective to include advocacy efforts, emphasising awareness of other actors in the medical, health care and scientific sector; empowering patients; and attracting the attention of policymakers and the media. The organisation was actively engaged in all phases of biomedical and clinical R&D. Box 1 illustrates this by showing the major contributions of VSN with regard to therapy.

Box 1: Major contributions of VSN to

Gene therapy: following scientific developments, informing patients

Stem cell therapy: following scientific developments, validating new therapies

Exon-skipping: setting-up science networks, following scientific developments

Enzyme replacement therapy: animal rights debates, clinical trials, compassionate use, reimbursement, newborn screening

Idebenone and TCH346: propagating clinical trials, informing patients

All in all, the VSN is a representative patient organisation that has a strong focus on R&D stimulation and steering. The VSN pursued this by investing in collaborative networks of scientists (see Fig. 1) who worked on gene location, gene identification, gene product identification, and productive enzyme therapy. Later, from the 1990s onwards the emergence of actual therapies resulted into including advocacy efforts, e.g. regarding compassionate use and reimbursement.

3. Involvement of patient organisations in biomedical and pharmaceutical R&D

In the pharmaceutical sector the innovation process is frequently characterised as a linear 'drug research and development pipeline'. The strictness of the model and its phases is created and emphasised by regulatory requirements and its accompanying milestones. Since the 1980s, several authors [13,14] have begun to claim that the linear layout of pharmaceutical innovation processes could be enhanced by feedback and feedforward steps. These interactions occur between different stages in which also other stakeholders, such as small high-tech companies and university hospitals are involved. Fig. 2 illustrates both the linear and the interactive models.

One category of external actors with whom pharmaceutical companies interact are the patient organisations, such as the VSN. In science, technology and innovation studies these representative user groups have been investigated over the last three decades [15,16]. The involvement of these organisations in innovation processes can be beneficial for several reasons [17]. These reasons are illustrated by examples taken from the history of the VSN:

1. *Overcoming market failure:* In the case of rare neuromuscular diseases the market does not adequately meet all societal problems and companies refrain from developing products that are commercially unattractive. For example, the VSN stimulated R&D on neuromuscular diseases by forming national and international networks of scientists.
2. *Employing knowledge of the users and their creative potential:* The VSN tried to gain access to the agenda-setting of scientific research by creating (inter)national networks of researchers. In this way they not only organised an efficient and effective knowledge exchange between scientists but also tried to convey the wishes, 'experiential knowledge' and priorities of patients.
3. *Enhance effectiveness (and speed) of the innovation process:* The VSN provided boundary conditions that contributed to the effectiveness of innovation processes. Some of its efforts focused on creating awareness and communicating information about new technologies, but it also included assisting with and initiating clinical trials, the management of expectations, representing patients towards regulatory agencies, and creating research projects. Moreover, the VSN also participated in the debate on the reimbursement of expensive biotechnology drugs.