Rare diseases: talk of the town for some time but what's next?

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Introduction

Rare diseases are defined as those whose incidence or rate of occurrence are so rare that they barely affect the common populace [1]. The incidence of disease is sometimes quite small compared to the luck-possibility of lottery drawing. However, it's a lottery that no one wants to win. Once it accidentally occurs to you, the disease may not lead to a long life, because of the frequent lack of treatment to support one's symptoms.

Because of their rarity, it is often treated with what the industry refers to as, 'orphan drugs'. The phrase "orphan drug" is frequently used to describe medical technology used to treat rare disorders [2]. These group of drugs are quite expensive because of the fewer number of people suffering from such sickness and usually provide low profit to manufacturer compared to other common drug for non-communicable diseases (NCD) as example. These characteristics might affect future investments in such drugs. Therefore, to aid in the funding of these drugs, legislative strategies are continuously being debated as to what criteria should be applied to the orphan drug policy in several countries.

This piece explores the different prioritisation criteria used for these orphan drugs in different countries. The objective of this piece is not to argue that severity must be considered as a priority setting criteria for rare disease, but rather to present the ethical underpinning of funding rare diseases and to facilitate the conversation among the decision makers to make orphan drugs more accessible as highlighted in the publication by Monica Magalhaes[3].

The remainder of this piece is structured as follows: first we highlight the different accepted definitions of rare diseases from different countries, which is followed by the challenges in prioritisation of rarity and the suggestion of a potential criteria for priority setting for rare diseases. Case studies from other countries are presented thereafter. Lastly, we present the ethical arguments for the reimbursement options for rare diseases and a proposal to investigate the potential of using severity as a priority setting criteria for rare disease in Thailand.

policy brief

What are "rare" diseases?

Nowadays, there is no universal definition of rare disease [1, 2, 4]. In most countries the definition of rare diseases is based on the number of cases per total population or prevalence thresholds. For example, in the United Kingdom, rare disease is a condition which affects less than 1 in 2,000 people [5]. Meanwhile, in Japan, it is described as disease with fewer than 50,000 prevalent cases [6].

In Thailand, the definition of rare disease has never been defined by law. The current data provided by National Health Security Office (NHSO) in Thailand in 2019 mentions rare disease as the disease which occur one with fewer than 10,000 cases, whereas an ultra-rare disease is defined as a disease with fewer than 1,000 cases [7].

Challenges with prioritising rarity

The problem of prioritising rarity or judging which disease is more deserving of attention is a difficult issue. Since treating rare illnesses usually requires exorbitant sums of money, they do not often qualify for public funding under the standard cost-effectiveness parameters. The fundamental principle of these parameters is to obtain maximum health benefits, regardless of who gets it [3]. Thus, paying an elevated price for the treatment of rare diseases does not agree with the maximising approach cost-effectiveness parameters [3]. However, cost-effectiveness alone does not capture all the elements of disease and illness [8]. In addition, prioritising rarity as a category will always be mired in social controversy. Equality will be a formidable challenge for any authority or system dealing with such cases to support this group of people [3]. The injustice in the allocation of large portions of the health care budget to minority people instead of others with common diseases makes it more challenging to prioritise rarity. Therefore, an alternative criterion is required for decision-makers.

If not rarity, what else?

Another approach that can be employed is to prioritise severity over rarity. The importance of shifting the focus to severity is well established in Norway, Finland, France and Germany. Simply put, severity matters because there is a moral reason to treat the ones that are worse off than others [8]. However, there are not well-defined internationally accepted criteria for defining severity. One example of a severity scale that can be employed in decision making was proposed by Nord E [9]. The following figure depicts the adapted proposed severity scale with the arrows representing the health gain from treatment for three hypothetical individuals. Upon prioritising severity rather than rarity, the health gain acquired by individual A would be valued more than the health gain acquired by individual B [10].

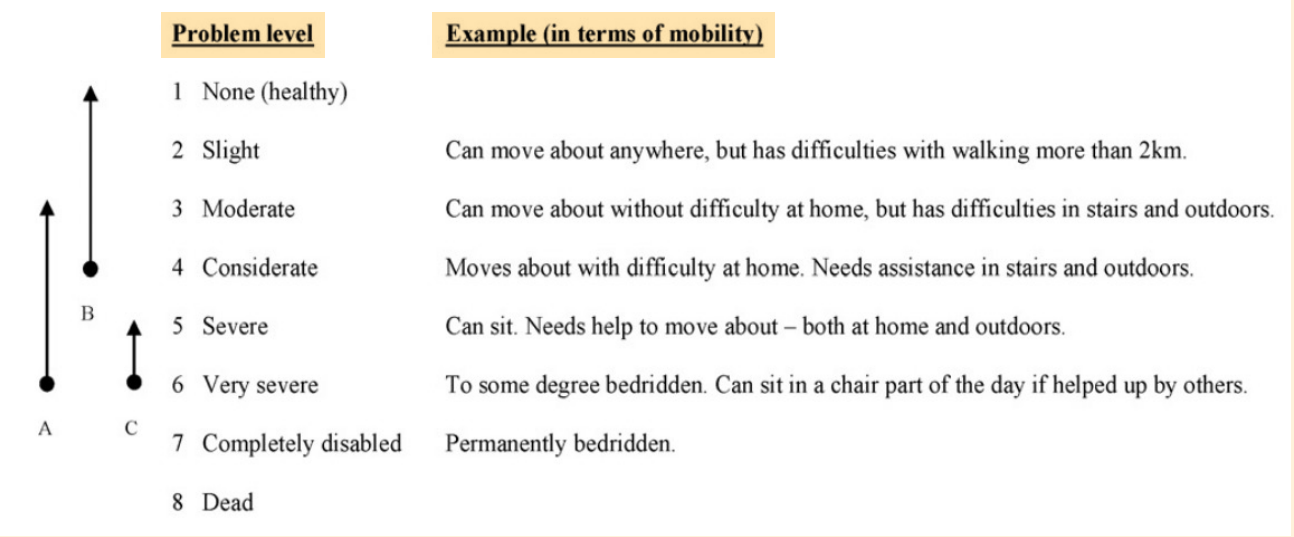

Figure 1. Severity scale proposed by Nord E [9].

Examples of prioritising severity over rarity

Successful examples from different countries prioritising severity over rarity are a testament to the possibility of a cost-effective implementation of such a strategy. One such example is Norway, where the severity of the disease is a component in drug coverage decisions [11].

In the context of rare disease, health inequalities can widen when heath maximisation is the only criteria for drug coverage decisions. To tackle this unfair distribution of health, Norway developed a system which considers the disease severity into the coverage decision of new drugs. Thus, in Norway, the following three priority setting criteria plays a key role in drug appraisal:

1. Health benefit
2. Resource use
3. Disease severity

In such a system, patients with very severe conditions have a stronger claim for treatment. Therefore, when all the other factors are equal, the ones with severe diseases often get higher priority.

In addition to Norway, the United Kingdom's National Institute for Health and Clinical Excellence (NICE) is an organisation that incorporates severity of the illness in the decision-making process [12]. For instance, during the appraisal of a drug, riluzole, used for the treatment of motor neuron diseases, the Technical Appraisal Committee (TAC) of NICE considered the "severity and relativity short lifespan" of affected individuals and subsequently recommend the use of this drug. Interestingly, this drug was approved despite its cost being higher than NICE's approved price range [13]. Similar examples of the NICE approving drugs and technology following considerations of severity has been reported. While, the severity of illness is not an explicit criterion in the decision-making process in the UK, there are examples where the TAC used severity as a criterion for drug appraisal. Although there are only a few countries in the world that have systematically incorporated concerns of severity into health technology appraisal, evidence from these countries points towards the feasibility of the approach.

Discussion

With a small potential market for such orphan drugs and no incentive for profit, such drugs often are very expensive when they find their way into the market. This high cost often makes these drugs non-ideal for public funding. The tension between the desire to yield maximum benefits from the finite resources and the rule of rescue makes the reimbursement of orphan drugs are subject of debate.

The utilitarian principle upon which cost-effectiveness heavily relies focuses on maximising the benefits for a fixed amount of money spent. Thus, funding these drugs goes against the utilitarian ethical view. On the other hand, the egalitarian ethical standpoint highlights the need for everyone to be treated equally and consequently posing an ethical imperative for the funding of rare diseases [14]. Additionally, some ethicists even agree that sometimes certain compensations are required, especially by the disadvantaged, in order to achieve equality [15]. However, this can lead to the using up of a significant amount of a finite public funds, thus leaving out another larger group of the population without access to healthcare. Therefore, the decision to choose rarity or severity as a parameter for public funding of drugs is not as black and white as it may seem.

In conclusion, considering the various ethical and moral trade-offs that are bound to occur, incorporating severity as an additional parameter in the decision-making process could be worth considering. The appropriateness of using this severity criteria can be witnessed from its successful incorporation into priority-setting by countries such as Norway and the United Kingdom. With Health Technology Assessment (HTA) at the heart of discussion around rare diseases, additional research is needed to access the effectiveness of using severity criterion in Thailand. However, undoubtedly it is time that we jump on the wagon to explore new and innovative policy changes that can make healthcare accessible to everyone. We hope that this piece promotes the much-needed discussion and collaboration between policy makers and researchers to enhanceaccess to rare and sever drugs.

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