

# A rare opportunity

Pharmacist, epidemiologist and expert in health outcomes research

**Dr Larry Lynd** unravels the complex issues surrounding support for orphan drug development, and describes his own rare disease research-focused career



## On a personal level, what inspired you to devote your career to researching rare diseases?

I wouldn't necessarily say I have devoted my whole career to rare diseases, but it's true that this component of my research is a big part of my wider research agenda, which involves health outcomes research and decision making relating to drug therapy. With my initial professional training as a pharmacist, I have been involved in pharmacotherapeutic management for many years. Following my practice experience in toxicology and a period of coordinating the provincial adverse drug reaction reporting programme, I developed an interest in epidemiology and health economics as methods for evaluating drug therapies, and ultimately generating information and integrating evidence to support both clinical and economic decisions.

Approximately four years ago, I was appointed to the British Columbia Ministry of Health Expensive Drugs for Rare Diseases Advisory committee on the strength of my health outcomes evaluation expertise. During this appointment I began to understand the nuances

of reimbursement decision making related to orphan drugs.

## Why is it that orphan drugs are so expensive, and how can it be explained that this cost continues to rise?

This is an important question that payers are continuously asking. Pharmaceutical companies will argue that the costs need to be high in order for them to make a return on their investment in R&D, given the small patient population, and to allow them to invest in future innovation and drug development that will lead to more treatments for more patients. They will also argue that society has to be willing to pay a premium for these drugs to support innovation and ongoing development. However, questions have been raised in general about how drugs are priced – whether this is based on the cost of goods plus some margin (as with goods in a usual market), or if they are they priced according to the cost the manufacturer believes the market will bear.

It is unfortunate that when an expensive drug for a rare disease is not funded, it is generally the payer that is seen as preventing the patient from gaining access to a particular therapy. However, a payer is making a decision within an environment of a limited budget, and must allocate resources across multiple competing priorities. More hard evidence relating to the rationale for pricing drugs at \$1 million per patient per year is needed to help justify public expenditure of this magnitude and to make industry more accountable for these excessively high prices.

## Can you explain how the societal value for the treatment of rare diseases can be determined?

Societal values can be determined using multiple methodologies, which is what we are currently doing as part of our work. Determining the extent to which society values the spending on expensive treatments

for rare diseases relative to the opportunity costs of funding expensive orphan drugs is best approached by combining insights arrived at using a range of different approaches.

## How is it decided whether a particular orphan drug should be funded?

These decisions are generally made by those responsible for drug budgets, either from a public or private payer. How the decision is actually made is not necessarily explicit and processes vary considerably. In fact, many jurisdictions don't have specific processes. Some jurisdictions do have specific and separate processes for orphan drugs, but even between these there is no uniformity. Thus, there are not any universally applied criteria that are used to inform decisions related to funding.

## Why does Canada lack a framework and priority-setting, decision-making model in terms of the demand for therapeutics to treat rare diseases and what are the consequences of this?

Canada has only recently developed a draft orphan drug framework that has yet to be tabled in Parliament. However, this framework differs from other orphan drugs regulations in that the most recent version doesn't include any financial incentives such as research concessions or tax breaks. Although it has been touted as 'improving access to orphan drugs', this framework will do little to improve access, because access is closely related to reimbursement decisions – particularly for orphan drugs, given their cost. As with many drugs that are not included as a reimbursable benefit that some patients could potentially pay out of pocket, orphan drugs will generally only be available for patients if they are covered by some payer (private or public). Thus, there is even greater pressure on the payers to fund, as there are no other alternatives.

# Minority medicine

Researchers from top Canadian universities; the **University of British Columbia**, **University of Ottawa**, **University of Toronto** and **McGill University**, are tackling the challenges posed by rare diseases, conducting research that will facilitate evidence-informed decision making

**A RARE DISEASE** is defined as any disease that affects a small percentage of the population. However, these diseases are anything but rare. In Europe and the US, there are an estimated 55 million people with a rare disease and the number of individuals affected varies from country to country. It is estimated that as many as 7,000 distinct rare diseases exist, many of them congenital. With the advent of personalised medicine, gene sequencing and the increased stratification of traditional classifications, more and more new rare diseases are discovered each year.

Rare diseases create a large and intricate problem for the provision of healthcare, centred on one pivotal fact: drugs for rare diseases are extremely expensive, often running to hundreds of thousands of Canadian dollars per patient, per year. This is consistent with the law of supply and demand in a typical market, and therefore not surprising in economic terms – but in moral and policy terms in the healthcare market, it is more complex. Canada maintains a mixed public/private healthcare system to serve Canadians 'according to their need' and 'irrespective of their ability to pay' – but should this extend to extremely high-cost drugs that will benefit a very small number of people and therefore are not cost-effective; a criteria that has been used to inform funding decisions relating to drugs for the past three decades? Thus, the primary issue is the extent to which policy makers should

prioritise spending for these expensive drugs for rare diseases within their limited budgets, given that in Canada provinces already spend almost 50 per cent of their budgets on healthcare.

## A FRAMEWORK FOR ACTION

Unfortunately, Canada has no framework for orphan drug regulatory approval at the federal level, and funding and reimbursement decisions related to drugs are made by provincial governments using heterogenous processes; what is covered in one province may be ignored by its neighbours, and the methods being used

Rare diseases are often referred to as 'orphan' diseases based on pharmaceutical companies' unwillingness to 'adopt' them – and indeed, this is a central issue in the debate; why should a company adopt a disease that does not present a suitable market?

to reach these decisions are often unclear. What is apparent, however, is the Canadian Government's need for accessible, relevant information on this topic, to help inform the development of a plan for future policy.

One team has stepped up to shoulder this challenge. Led by Dr Larry Lynd, the New Emerging Team for Rare Diseases is composed of internationally recognised Canadian researchers, and with \$1.5 million in funding from the Canadian Institutes of Health Research (CIHR), they aim to investigate tenable reimbursement methodologies and policies to support decision making for the treatment of rare diseases. The researchers will add value to the Canadian healthcare system in three ways: firstly, by ascertaining the societal value of rare disease treatment; secondly, by clarifying the present and future challenges presented by rare diseases and; finally, by exploring new approaches to drug development and pricing.

## GAUGING OPINION

In British Columbia, the cost of medication for mucopolysaccharidosis type one (MPS I) is approximately \$435,000 per patient, per year. This medication does not cure the disease, but simply mitigates symptoms, improving patient quality of life. In the first strand of their research, Lynd and his collaborators are attempting to decipher the extent to which the Canadian public

## INTELLIGENCE

### DEVELOPING A CANADIAN FRAMEWORK FOR EVALUATION AND DECISION MAKING FOR EXPENSIVE DRUGS FOR RARE DISEASES THROUGH INNOVATION, VALUE AND PRIORITY SETTING

#### OBJECTIVES

To undertake collaborative translational research with the objective of helping to inform the development of drug coverage decision-making models relating to government funding of drug therapy for rare diseases.

#### TEAM MEMBERS

Dr Jan Friedman; Dr Stirling Bryan; Dr Craig Mitton; Dr Sandra Sirrs; Dr Lorne Clarke; Dr Carlo Marra; Peter Klein, University of British Columbia • Dr Doug Coyle, University of Ottawa • Dr Yann Joly; Dr Bartha Maria Knoppers, McGill University • Dr Fiona Miller, University of Toronto • Barbara Walman; Dr Eric Lun; British Columbia Ministry of Health Services • Barry Jones, Health Canada • Dr Tammy Clifford, Canadian Agency for Drugs and Technologies in Health • Bob Nakagawa, College of Pharmacists of British Columbia

#### FUNDING

Canadian Institutes of Health Research (CIHR)

#### CONTACT

##### Dr Larry Lynd

Associate Professor and Associate Director of the Collaboration for Outcomes Research and Evaluation (CORE)

Faculty of Pharmaceutical Sciences  
University of British Columbia  
4110-2405 Wesbrook Mall  
Vancouver, British Columbia  
V6T 1Z3, Canada

T +1 604 827 3397  
E larry.lynd@ubc.ca

<http://rare-diseases.ca>  
<http://core.ubc.ca/>

DR LARRY LYND received his degree in Pharmacy (BSP) from the University of Saskatchewan and went on to complete a doctorate in the Department of Health Care and Epidemiology at the University of British Columbia in 2002. He held a two-year doctoral fellowship in health economics at McMaster University. Lynd is now an associate professor in the Faculty of Pharmaceutical Sciences and Associate Director of CORE. He is also a scientist at the Centre for Health Evaluation and Outcomes Sciences at the University of British Columbia, and at the Centre for Clinical Epidemiology and Evaluation in Vancouver, Canada.

is willing to prioritise this treatment, potentially at the expense of treatment for more common diseases, or other societal initiatives. To do so, in a survey involving 2,000 respondents, the team has engaged Canadians directly.

The results have been very telling. Respondents were asked to choose between allocating funding to a common or rare disease, and to rate five statements about rare diseases. 60.05 per cent of participants strongly agreed with the statement 'everyone should have equal access to healthcare, regardless of cost', but the amount they were willing to pay for a high-efficacy treatment varied considerably. Although willing in spirit to support high costs, what they said they were willing to pay was well below the annual cost of MPS I treatment, and many others.

#### RANKING RARE DISEASE

Canadians were also asked to choose between alternative funding scenarios in which resources could be allocated to either treat patients suffering from a rare disease or to other uses, such as the treatment of a more common disease, or a greater societal benefit such as educational and recreational programmes. While most respondents chose to fund the treatment of rare disease patients instead of public goods like schools and community centres, they also tended to prioritise treating the larger number of common disease patients that could be cared for with the same amount of funds. A majority of respondents did favour allocating the funding to the rare disease option in some situations. In short, Canadians did not appear to prioritise the funding of rare disease treatments just because the diseases are rare, but did favour prioritising the treatment of these diseases if there is an unmet need, they are severe and life threatening, or affect children; features which characterise many rare genetic disorders.

In addition to choosing between a set of specific scenarios for allocating resources, respondents to the survey were also asked to rank a set of 13 general principles relevant to healthcare prioritisation in order of importance. The rarity of a disease was included in this set of values in order to explore the relative importance Canadians attach to disease rarity in a more abstract context. The results of this task were consistent with the preferences expressed by respondents in choosing between scenarios. While rarity was ranked as the second least important factor by this sample of Canadians, the highest ranked values were the safety and efficacy of the drug in question and the severity

of the disease it is meant to treat, which are the dominant principles used by decision-making bodies in deciding which drugs deserve coverage. Together, the results have enabled Lynd and his co-investigators to build a detailed picture of Canadian priorities with regard to rare diseases that suggests the Canadian public does not favour special treatment for orphan drugs due to the rarity of the diseases they treat, but does open the door to special consideration based on the severity of the disease or the alternatives available to the patient.

#### WIDER WORK

In order to address the second strand of their project, Lynd's group is undertaking the Informing Future Orphan Drug Coverage Using Scenario Studies (iFocuss) project. This initiative will centre on the development of potential future scenarios, and then examine how decision makers might deal with future decisions using focus groups comprised of current stakeholders. Through this activity, it is hoped the researchers will be able to derive some best practices for use going forward, which will be of significant value to present policy makers – who would otherwise effectively be blind to the issues at stake, and the pitfalls to avoid.

Finally, the CIHR team will examine best practice in the pharmaceuticals industry. Rare diseases are often referred to as 'orphan' diseases based on pharmaceutical companies' unwillingness to 'adopt' them – and indeed, this is a central issue in the debate; why should a company adopt a disease that does not present a suitable market? Prices must remain high to support research and development costs and promote further innovation, companies argue. In order to help overcome this otherwise insoluble problem, the CIHR researchers will investigate how regulations surrounding clinical trials could be safely altered in the context of rare disease drugs. This will be achieved through comparative literature reviews of academic texts as well as international clinical trial regulations.

#### THE FUTURE OF ORPHANS

Orphan diseases may well be among the thorniest problems faced by health policy makers today, but thanks to the work of Lynd and his group, the Canadian governments will be much better prepared to face this issue going forward. Perhaps, in time, this issue can be resolved without disturbing the country's noble goal of providing healthcare for every citizen in need.

