Rare Diseases: Canada's "Research Orphans"

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Although definitions vary by jurisdiction, diseases affecting approximately 1 in 2000 people are considered rare.[1] Canada is one of few developed countries without a national "orphan drug" program to protect rare disease patients facing exorbitant drug costs. Public debate over government funding for these drugs is periodically stimulated by stories of patients who are deprived of life sustaining therapies due to cost. However, most Canadians remain unaware of an even more impactful disparity between common and rare disease care in this country - the availability of research funding. Far from worrying about expensive therapies, patients receiving a rare disease diagnosis are surprised to learn that there is limited scientific knowledge about the causes and natural history of most of these diseases, and often little or no ongoing research.

The reasons for this are several fold. Public funding agencies have a mandate to improve public health, which naturally favours grants that address common conditions. As a result, rare disease researchers entering open grants competitions may be disadvantaged by the limited impact of their potential findings.[2, 3] Furthermore, small sample sizes make it difficult for researchers to recruit and study an adequate number of patients to reach scientifically valid conclusions. As a result, even basic knowledge about the diagnosis, causes, and consequences of many of these diseases is lacking.[3] Even when these aspects are well understood and drug development can be considered, the pharmaceutical industry often opts out because development costs are difficult to recuperate from the small number of potential recipients.[4]

The greatest impact on this inequity has been made through government legislation. In 1982, the U.S. Food and Drug Administration (FDA) established the Office of Orphan

Products Development to promote development of products for the diagnosis and/or treatment of rare diseases. The Orphan Drug Act, passed in 1983, created financial incentives for academic institutions and manufacturers to engage in rare disease drug development, including tax credits for costs of clinical research, a waiver of certain fees involved in new drug applications, direct FDA grant support, assistance for clinical research, and a seven-year period of exclusive marketing for successful products.[2] Since this law was passed, over 300 rare disease products affecting over 14 million Americans have come to market, compared to fewer than 10 products in the decade prior.[5] The Rare Diseases Act, passed in 2002, included provisions for a new rare disease grants network, support for research in diagnostic tools for patients with rare diseases, and development of regional centers of excellence for clinical research and training in rare diseases.[6] Finally, the US National Institutes of Health created the Rare Diseases Clinical Research Network in 2003, with a budget of US $71 million to fund multi-national rare disease studies.[2, 7]

In the European Union (EU), the "Framework Programmes" (FPs), the EU's main instrument for research funding, have sequentially increased rare disease research funding over the past two decades. The 5th FP (1998 - 2002) funded 47 rare disease projects for a total of 64 million euros, FP6 (2002 - 2006) funded 59 projects for 230 million euros, and the current FP7 (2007-2013) is on track to surpass this total.[8] The EU has also addressed the issue of orphan drug development specifically. In 1999, the European Parliament adopted the Regulation on Orphan Medicinal Products, guaranteeing 10 years of market exclusivity for approved orphan products, facilitating their registration by creating an EU-wide approval procedure, and calling for tax credits

to be developed by individual member states.[5] Individual EU countries were not far behind, with Germany committing 25 million euros to a new rare disease research strategy in 2003, Spain allocating 11.9 million euros to a new program in 2003, and France creating a rare disease consortium funded by both government and private charities with a 7.9 million euro budget in 2002, and launching the French National Plan for Rare Diseases, with 20 million euros dedicated to rare disease research funding between 2005-2008.[1]

Other developed nations have also risen to the challenge. The Singapore Government approved an Orphan Drug Act 1991, the Australian Orphan Drug Policy was established in 1997, the Taiwanese "Rare Disorder Prevention/Treatment and Pharmaceutical Law" was implemented in 2000, and the Japanese Orphan Drug Regulation was approved in 1993, guaranteeing 10 years of marketing exclusivity to successful drug developers.[1, 3, 5]

Canada remains one of the few developed countries without a comprehensive rare disease policy to address research into rare diseases, drug development incentives, and drug access for patients. Since it came into existence in 2000, the Canadian Institutes of Health Research has seen an annual budget increase from around $350 million to nearly $1 billion in 2009-10. Yet it was not until 2011 that the first rare disease-specific competition was announced, allocating a maximum of $14.5 million between 2012-17, including commitments from partner organizations.[9]

In our limited resource environment, a utilitarian approach to wealth distribution would argue that substantial resource investment in rare diseases fails to maximize the benefit to society by bringing the greatest good to the greatest number. However, the "paradox of rarity" is that with over 6000 known rare diseases and 6-8% of the population affected by a rare disease, even though each disease is rare, rare diseases patients are many.[10]

Based on a belief that our society's moral obligation is to protect each individual's rights, The Canada Health Act upholds the principle of "non-abandonment," whereby all Canadians should have "timely access to health services on the basis of need, not ability to pay..." and "the health care services available to Canadians are of high quality, effective, patient-centered and safe."

Far beyond the simple question of access to drugs, a right to effective and high-quality care can not be fulfilled without addressing the fundamental gap in access to scientific advancement and research in rare diseases. It is time for our federal leaders to join the rest of the developed world in legislating a comprehensive strategy to enable orphan disease research. In addition to sustained public attention, efforts by the Canadian clinicians and researchers will be required to drive a political solution.

References