National Strategy for High-Cost Drugs for Rare Diseases

Canadian Cancer Society's submission to Health Canada

March 2021

The Canadian Cancer Society (CCS) appreciates the opportunity to participate in the development of the national strategy on high-cost drugs for rare diseases. CCS is pleased that Health Canada is working to establish a national strategy for high-cost drugs for rare diseases, including oncology drugs by investing up to $500 million per year to help Canadians with rare diseases access the drugs they need. Our submission highlights the unique challenges facing people with rare cancers, their families, caregivers, clinicians and researchers. We also provide potential solutions that may help to offset some of the challenges faced by those with rare cancers.

About us

CCS is the only national charity that supports Canadians with all cancers in communities across the country. No other organization does what we do; we are the voice for Canadians who care about cancer. We fund groundbreaking research, provide a support system for all those affected by cancer and shape health policies to prevent cancer and support those living with the disease.

Background

Rare cancers are not rare at all. Despite the relatively low incidence of each type of cancer, rare cancers (those that are <6 per 100,000) combined account for approximately 25% of cancer cases in Canada.[1] The lack of an internationally agreed upon definition of a rare cancer makes it challenging to understand the magnitude of the cancer burden, however, some estimates suggest the proportion to be as high as 52.5% using different definitions of rare (if consider those that are 15 per 100,000).[2] Several groups worldwide have estimated that 1 in 4 individuals diagnosed with cancer will have a rare cancer in their respective geographic regions.[3] Survival rates for rare cancers are lower than those for common cancers (5 years; 56.6% vs. 68.8) in Ontario.[4] Five-year survival for rare cancers are similar to those reported in Europe (47%) [5] and Italy (55%). [6]

[1] Brenner, D.R., Weir, H.K., Demers, A.A., Ellison, L.F., Louzado, C., Shaw, A., Turner, D., Woods, R.R. and Smith, L.M., 2020. Projected estimates of cancer in Canada in 2020. *Cmaj*, *192*(9), pp.E199-E205.

[2] Walker, E. V., Maplethorpe, E., & Davis, F. G. (2020). Rare cancers in Canada, 2006–2016: A population-based surveillance report and comparison of different methods for classifying rare cancers. *Cancer epidemiology*, *67*, 101721.

[3] G. Gatta, J.M. van der Zwan, P.G. Casali, S. Siesling, A.P. Dei Tos, I. Kunkler, *et al.* RARECARE working group. Rare cancers are not so rare: the rare cancer burden in Europe Eur. J. Cancer, 47 (17) (2011), pp. 2493-2511

[4] Ontario Health (Cancer Care Ontario). Ontario Cancer Statistics 2020. Toronto: Ontario Health (Cancer Care Ontario); 2020.

[5] Gatta G, van der Zwan JM, Casali PG, Siesling S, Dei Tos AP, Kunkler I, et al.; RARECARE working group. Rare cancers are not so rare: the rare cancer burden in Europe. Eur J Cancer. 2011 Nov;47(17):2493-511.

[6] Trama A, Mallone S, Ferretti S, Meduri F, Capocaccia R, Gatta G; RITA working group. The burden of rare cancers in Italy: the surveillance of rare cancers in Italy (RITA) project. Tumori. 2012 Sep-Oct;98(5):550-8.

Rare cancers pose all the main problems that are typical of rare diseases. They also present people with cancer, their families, clinicians, researchers and policy makers with profound challenges. Rare cancers affect:

1) clinical decision making: people with rare cancers, sometimes known as "forgotten cancers" pay a steep price as a result of repeated misdiagnoses and inappropriate treatment
2) healthcare organization: those living in rural and remote communities may need to travel long distances to get the necessary care and face challenges in finding the necessary information about their rare cancer
3) clinical research: due to lack of sufficient evidence, insufficient funding and a low number of research participants.

Rare cancers also disproportionately affect younger and minority populations.[7]

The section below describes a brief story of a person with a rare cancer and his challenges within the Canadian healthcare system. See Appendix 1 for the full story.

This story aims to shed light on the struggles of a person with a rare cancer and an opportunity for policymakers to recognize the current gaps and barriers that prevent people, like Andy to receive the care they deserve.

A new normal for Andy Harris after a rare cancer diagnosis

Andy spent 2015 feeling tired and having a lot of unexplained pains, particularly in his left groin. Though his doctor wrote it off, Andy knew something was wrong. Andy was diagnosed with metastatic adenocarcinoma of unknown primary origin, a type of cancer that starts in gland cells that make up the inner lining of some organs that spread before it was found, so doctors didn't know its exact origin. His oncologist told him he had six months to live, a year at most, and thought treatments wouldn't help

"This doctor said they couldn't cure me, but they could treat me," says Andy. "You have no idea how much hope that gave me after initially being given a short time to live."

Armed with a chance of living longer, Andy began a demanding treatment schedule towards the end of 2016 that involved 35 specialists, eight different hospitals and four surgeries.

"Being unique is not a good thing when it comes to cancer. Cancer of unknown primary accounts for only 2 to 5 % of all cancer cases. I need to live with never knowing if or when cancer may return," says Andy, who was diagnosed with metastatic adenocarcinoma of unknown primary in 2016.

Full story can be found in Appendix 1.

[7] Shin DW, Cho J, Yang HK, Kim SY, Lee SH, Suh B, Shin HY, Lee HJ, Kim DG, Park JH. Oncologist perspectives on rare cancer care: a nationwide survey. Cancer research and treatment: official journal of Korean Cancer Association. 2015 Oct;47(4):591.

Response to Health Canada's discussion paper on National Strategy for High-Cost Drugs for Rare Diseases

Health Canada has proposed potential solutions for the major issues identified for a national rare disease strategy in the discussion paper for this consultation.[8] CCS believes the best approach includes the implementation of all 13 proposed actions. To move forward in the development of a national strategy, we highlight key solutions that will help to improve care for people with rare cancers.

Issue 1: How to improve patient access to high-cost drugs for rare disease and ensure that access is consistent across the country?

1.1. A single framework for decision making on high-cost drugs

The development of a single framework for decision making on high-cost drugs will allow for a consistent approach in which high-cost drugs for rare diseases, including rare cancers, should be covered and which patients should be covered under the relevant conditions.

1.2. Health Canada regulatory approval

To improve patient access to high-cost drugs and consistent access across the country, it is critical to develop a coordinated process for the market authorization and reimbursement of drugs for rare diseases. The process of identifying a potential new drug and making it available to Canadians can take many years. This process is long and can be torturous for people with cancer and their families. While many rare cancers remain untreatable and cause much suffering and premature death, there have been instances where drugs are approved in the United States and Europe, but not in Canada. Even when drugs are approved in Canada, more than 95% do so after approval in the United States or Europe. Submissions to Health Canada for 84% of rare disease treatments approved between 2002-2016 were filed after these submissions were filed with American and European regulators. Additionally, 23 of these treatments for rare diseases were not approved in Canada while they were approved in the United States or Europe.[9]

Patients have no choice but to wait for long periods of time and have great uncertainty as to whether they will be able to access the treatment. This can result in extreme distress for the person with rare cancer and their families. While CCS supports the Canadian government in ensuring drugs are affordable and accessible, limiting access to costly drugs increases barriers to high-quality care for people with cancer.

<u>Special Access Program (SAP)</u>

Currently, patients seeking access to treatments that are not approved by Health Canada, patients work with their physician to navigate Heath Canada's special access program. Although this was initially developed as an exceptional mechanism, the SAP has become the access pathway for many rare disease patients because treatments they need are not available through the standard access pathway. This program is not the ideal mechanism for

[8] Government of Canada. Building a National Strategy for High-Cost Drugs for Rare Diseases. A discussion paper for engaging Canadians. 2021 Retrieved from: https://www.canada.ca/en/health-canada/programs/consultation-national-strategy-high-cost-drugs-rare-diseases-online-engagement/discussion-paper.html

[9] Rawson, N., "Regulatory, Reimbursement, and Pricing barriers to accessing Drugs for Rare Disorders in Canada", Fraser Institute, 2018: https://www.fraserinstitute.org/sites/default/files/barriers-to-accessing-drugs-for-rare-disorders-incanada.pdf.

facilitating access to treatment. It can be time-consuming and requires patients to rely on their physician to seek approval from Health Canada by providing the scientific literature that demonstrates it is the right solution for the patient. This program does not come with reimbursement, leaving patients to find their own ways to pay for an extremely expensive treatment.

These gaps in the Canadian regulatory and review process have to be addressed so that people with rare cancers are able to receive the treatment they need.

1.3. Patient, clinician and caregiver engagement

Patients and clinicians are at the frontlines of receiving and providing treatment. Given the limited knowledge available about rare cancers and their treatments, experts with real-life experience need to be involved at all stages. Decision-making processes should seek input of clinical experts who have experience with patients with rare cancers.

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>
> "Getting a second chance at life is the best lottery anyone could win and I feel truly lucky to have been given one."

It is also extremely important to hear from patients. Patients are able to offer a range of perspectives that can contribute to evaluating the treatment. They have perspectives on the burden of illness, impact of the disease on their day-to-day life, most challenging aspects of their condition, unmet medical needs and experience with treatments. People with rare cancers, like Andy, often become experts in living their condition, given the limited information available. Platforms for engagement for patients and clinicians will also increase awareness of programs and policies related to accessing high-cost drugs for rare diseases.

In addition to patient and clinician engagement, caregivers should also be engaged to provide input as they are regularly the voice of the person with cancer and have key insights on navigating with to receive access to treatment.

1.4. Funding for research on rare diseases in Canada

Due to limited research, people with rare cancers have limited treatment options. Funding for research provides an opportunity for researchers to develop improved mechanisms for diagnosis and innovative treatment options for those with rare cancers. This will increase knowledge of rare cancers affecting Canadians and lead to new discoveries resulting in improved health outcomes. Health Canada should also explore the opportunity to provide drugs to people with rare cancers through clinical trials, which can sometimes be the only hope for treatment. CCS is committed to funding research for rare cancers. In 2019/20, CCS invested $8.03 million in research on rare cancers. Our total investment in rare cancers from 2015-2020 is close to $40 million.

Issue 2: How to ensure decisions on covering high-cost drugs for rare diseases are informed by the best evidence available?

2.1 Health Technology Assessments for rare cancers[10]

After the regularly approval, access to a new drug depends on successfully passing the Canadian Agency for Drugs and Technologies' pan-Canadian Oncology Drug Review (pCODR) expert review committee recommendations (pERC). pERC's framework does not explicitly address rarity. Adopting processes, criteria and standards that are more appropriately suited for assessing rare disease treatments are key to improving access. Applying the same standards to drugs for rare diseases may not be appropriate considering the additional barriers that come with the research of rare cancers. These include lack of RCTs and comparative data, no appropriate standard of care and uncertainty in burden of illness.[11] It is important to explore how rarity can be incorporated in the oncology health technology assessments (HTA) in Canada. While pERC's membership consists of experts in oncology across Canada, we recommend the inclusion of rare cancer expertise to shed light on the challenges in clinical cancer care for those with rare cancers. This additional layer of expertise can provide insights to facilitate the development of processes, criteria and standards that are more appropriately suited for those with rare cancers.

2.2 Increase real-world evidence through existing patient registries

Real-world evidence has been gaining prominence as a methodology that can be used to evaluate drugs in conjunction with randomized control trials when there is limited evidence. There is limited research on rare cancers and even less research on the treatment options for those with rare cancers. The establishment of patient-reported outcome measures (PROMs)as part of patient registries is key in the development of drug policy for rare diseases.

Robust databases allow monitoring of disease progression, effects of treatment and outcomes.[12] They also help track patients' health, recruit patients for clinical trials, and supplement data from traditional clinical trials to determine patient safety, efficacy and side effects of drug treatment.[13] Robust data feeds into improving our research on rare cancers which can improve care in diagnosis, treatment and prognosis and can also lead to new discoveries about the pathogenesis of these diseases.

The use of (PROMs) can be key to helping researchers understand how diseases and treatments impact quality of life and symptoms. PROMs can be used in research to provide a patient perspective. While rare diseases pose a number of additional challenges in utilizing PROMs (ie. small sample sizes), researchers suggest that they will provide a more complete picture of the experiences of those with rare diseases. [14]

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[10] The Canadian Forum for Rare Disease Innovators. Unique Approach Needed: Addressing barriers to accessing rare disease treatments. Retrieved from https://www.ourcommons.ca/Content/Committee/421/HESA/Brief/BR10189782/br-external/CanadianForumForRareDiseasesInnovators-e.pdf

[11] Keech J, Dai WF, Beca J, Chan K. The impact of rarity on oncology health technology assessment (HTA) funding in Ontario: A review of pCODR recommendations from 2012-2017. 2019. Retrieved from https://cadth.ca/sites/default/files/symp-2019/presentations/april16-2019/E7-presentation-jkeech.pdf

[12] Is the current approach to reviewing new drugs condemning the victims of rare diseases to death? A call for a national orphan drug review policy. *Clarke JT. CMAJ. 2006 Jan 17; 174(2):189-90.*

[13] Boycott KM, and Ardigo D. 2018. Addressing challenges in the diagnosis and treatment of rare diseases. Nature Reviews Drug Discovery, 17(3): 151–152.

[14] Slade A, Isa F, Kyte D, et al. Patient reported outcome measures in rare diseases: a narrative review [Published online April 23, 2018]. *Orphanet J Rare Dis.* doi: 10.1186/s13023-018-0810-x.

This data could also be collected on drug for rare diseases with continuous monitoring and evaluation on its benefits to people with rare cancers. This would incentivize manufacturers to develop innovative treatments to continue to receive payments for the treatments approved in the market. The National Institute for Health and Care Excellence (NICE) in the United Kingdom recently implemented such a change to its HTA recommendation framework. If a drug has potential to satisfy the criteria for routine using commissioning but significant clinical uncertainty remains, it can be made available earlier via the Cancer Drug Fund. The drug remains available while more evidence is gathered to resolve key areas of uncertainty and show that the drug works in the population in the United Kingdom. The data collection period is limited and data must be able to inform an update to the recommendation.[15]

2.3 International collaboration

Many rare tumours can be incurable. However, with limited support for people with cancer, it can be difficult to conduct clinical planning. International collaboration is necessary to carry out clinical trials of adequate statistical power to answer significant questions in a timely fashion. Enabling health data sharing in Canada and across international borders can be critical for those with rare cancers to benefit from better healthcare and to benefit from better healthcare and from new research outputs. This international network can help physicians in Canada learn from other physicians around the world to improve care for their patients.

Issue 3: How to ensure spending on high-cost drugs for rare diseases does not put pressure on the sustainability of the Canadian healthcare system?

Developing treatments for cancers is extremely costly, let alone treatments for rare cancers. Under the current regulations by the Patented Medicines Prices Review Board (PMPRB), there are limited incentives for manufacturers to bring rare disease drugs to the Canadian market. This should be considered as part of the development of the national rare disease strategy.

3.1 Sharing of costs and pooling of risks

Sharing costs and pooling of risks is the best approach to ensure spending on high-cost drugs does not add pressure to the already pressured Canadian healthcare system. Working collaboratively with manufacturers is key to making sure we are able to access the care we need.

3.2 International governments

There may be an opportunity to explore collaborations with international governments to jointly address this global issue.

Conclusion

We recognize there is no easy solution. However, there are several actions can be implemented simultaneously to improve access to treatment for people with rare cancers who represent 25% of Canadians diagnosed with cancer every year. We thank you again for the opportunity to provide our input and look forward to the development of the strategy. We are keen to continue to engage on conversations on rare diseases with Health Canada on this

[15] Lye E, Binder L, Elias M, Sit C. Improving access to innovative cancer therapies in Canada. 2018. Retrieved from https://survivornet.ca/wp-content/uploads/2018/04/wp-_improving_access_to_innovative_cancer_therapies_in_canada.pdf

topic to help support people with rare cancers receive the timely and equitable access to high-quality care across Canada.

Appendix 1. A new normal for Andy Harris after a rare cancer diagnosis

Andy spent 2015 feeling tired and having a lot of unexplained pains, particularly in his left groin. Though his doctor wrote it off, Andy knew something was wrong. In June 2016, the pain moved up to the left side of his pelvis, which his doctor believed to be an infected lymph node. When the lymph node became enlarged, they decided to remove it with surgery.

Two weeks later, a follow-up pathology report revealed the truth. Andy was diagnosed with metastatic adenocarcinoma of unknown primary origin, a type of cancer that starts in gland cells that make up the inner lining of some organs that spread before it was found, so doctors didn't know its exact origin.

His oncologist told him he had six months to live, a year at most, and thought treatments wouldn't help. Not willing to give up, Andy advocated for himself, and asked for a second opinion, and his new oncologist set him up with a surgeon and multiple PET Scans. Further tests didn't find the origin of the cancer, but the PET scans revealed cancer in his left pelvis, a 5.3 cm tumor and several cancerous lymph nodes in his pelvis and groin.
"This doctor said they couldn't cure me, but they could treat me," says Andy. "You have no idea how much hope that gave me after initially being given a short time to live."

Armed with a chance of living longer, Andy began a demanding treatment schedule towards the end of 2016 that involved 35 specialists, eight different hospitals and four surgeries. First, Andy endured six rounds of chemotherapy in hopes of shrinking his tumour and cancerous lymph nodes. After chemo, he was sent to have major surgery to remove the tumour, which had grown around his left femoral vein, followed by radiation to clean up what was left behind.

In October 2017, Andy experienced a recurrence when he discovered a lump in his left groin and this time surgery was not the optimal choice given all the previous interventions. Thanks to new research and meeting all the qualifications, Andy decided to enroll in a clinical trial in immunotherapy. However, when his cancer kept growing he had to stop the trial and had a fourth surgery to remove the tumour in June 2018.

Since then, Andy has been on surveillance, meaning quarterly CT scans and checkups. He is also dealing with long-term side effects with permanent damage in his left leg and lymphedema, a swelling resulting from removal or damage of his lymph nodes during treatment. He is currently working on living well with medical follow-ups and ongoing recovery both mentally and physically, while trying to function in what he calls the "new normal" after diagnosis.

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