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COMMENTARY

Clinician participation in CADTH's pan-Canadian Oncology Drug Review: contribution and impact on cancer drug funding recommendations

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In any given week, media headlines publicize the benefits of a new "breakthrough" cancer drug, with patients and clinicians subsequently advocating for its use. Governments, which face the difficult task of deciding how best to allocate limited public resources, must at the same time balance ongoing commitments to provide optimal health care for Canadians and to ensure value for money and the sustainability of the Canadian health care system.

Established by the provincial and territorial ministries of health, the pan-Canadian Oncology Drug Review (pCODR) program operating within the Canadian Agency for Drugs and Technologies in Health (CADTH) is designed to bring consistency and clarity to the assessment of cancer drugs by looking at clinical and economic evidence, by taking into consideration clinician and patient perspectives, and by using that information to make recommendations to the participating jurisdictions to guide their drug funding decisions[1].

The cancer drug review process (Figure 1) begins when a pharmaceutical manufacturer or a group of cancer experts in a particular area of cancer, called a tumour group, submits for review a new drug or a drug for a new indication. The submitter is required to provide information about the drug's clinical benefit and cost-effectiveness.

An essential part of the pCODR process is founded on the principles of representation and collaboration. When a drug submission is accepted, registered patient groups can make a patient evidence submission on a drug undergoing review. The process integrates patient perspectives from those cancer patients and family members who could be directly affected by the recommendation. As of 31 December 2016, 97% of reviews have had patient input.

To further build upon the principles of representation and collaboration, CADTH introduced, on 1 February 2016, a pilot project for clinicians (practicing oncologists) not part of the review team panel to participate in the pCODR process by providing input on their clinical experience in the clinical communities across Canada to help the pCODR Expert Review Committee (PERC) gain insights into regional and local practice issues, and to identify areas of unmet need[2]. Examples include identifying key benefits and harms of the drug under review observed in the real-world clinical setting, determining the place of the drug under review within the current treatment paradigm, and identifying whether companion diagnostic testing is required for the new drug under review, among other practice issues. As of 31 December 2016, 91 clinicians had registered for the pilot, and 75% of 16 reviews had included clinician input. This pilot project will be evaluated in 2017 after 25 cancer drug submissions with clinician input have been received.

A key contributor to the new pilot project, the Medical Advisory Committee (MAC) of Lung Cancer Canada provided clinician input on six reviews over 12 months. In the lung cancer community, MAC members have seen multiple new and effective drugs for non-small-cell lung cancer over the last few years. When the trials are reported through the extensive medical media, conference proceedings, professional meetings, and social media, clinicians and patients both become aware of the advances and seek rapid access to the new drugs.

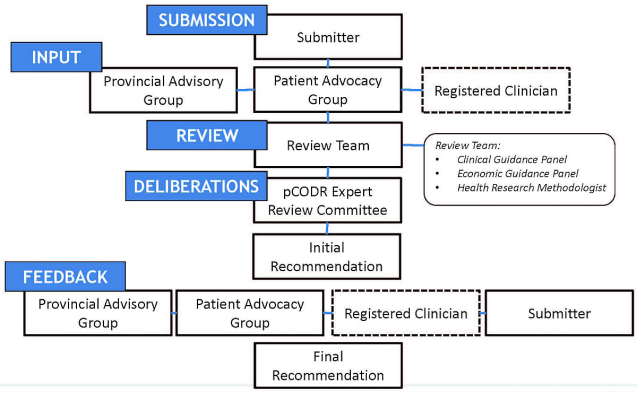

FIGURE 1 The pan-Canadian Oncology Drug Review process.

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By working in collaboration with other thoracic medical oncologists across the country, coordinated through the MAC, the group is able to swiftly and effectively identify physicians experienced with the drug under review by the pCODR program. A member of the MAC takes the lead in drafting the clinical input submission, and other members are invited to review the submission, make suggestions, and put their names to it in support. Rather than simply repeat the presented efficacy information provided by the submitter, clinician input seeks to contextualize the findings: for example, where will this new drug fit into the patient's treatment options, how many patients might be eligible, what are the alternatives, and what are the benefits (among many other areas of discussion).

Although clinician input can come from a single registered physician, a larger group working collaboratively through the MAC is able to build a stronger case to help inform the recommendation through their broad shared experiences with the drug.

Input is also received from the Provincial Advisory Group (PAG)[3] to ensure that the pCODR drug review process and the resulting recommendations meet the needs of the participating jurisdictions for evidence-based recommendations that guide drug funding decisions. Input brought forward by PAG can include implementation considerations such as patient accessibility, drug wastage, and health care resource utilization, among other issues.

Once a submission for a cancer drug has been initiated, the pCODR program draws on leading experts from across Canada to conduct the clinical and economic evaluation of the drug. Individuals who participate on the Clinical Guidance Panel bring expertise in the type of cancer targeted by the drug, and individuals on the Economic Guidance Panel have experience in applied health technology assessment and health economics. The Clinical Guidance Panel is also supported by methodologists who conduct a systematic review of the clinical literature and provide a critical appraisal of the included studies.

With regard to the clinical expertise formalized by the pCODR program, the Clinical Guidance Panels represent expertise in a specific tumour site: breast; endocrine; gastrointestinal; genitourinary; gynecologic; head-and-neck; leukemia, lymphoma and myeloma; lung; melanoma; neurologic; and sarcoma. In cases in which a drug is used to treat a tumour not addressed by any of the named panels, pCODR will form an ad hoc expert panel[4]. Each panel that conducts a review consists of 3–5 cancer specialists from across Canada, recognized as experts for that specific tumour site, who interpret the clinical data, provide context, and develop the main conclusions of the Clinical Guidance Report.

The impetus for the submission of a pCODR review is usually the results of a clinical trial suggesting clinical benefit from a drug for a particular patient population. Sometimes, more than one clinical trial has provided evidence that is directly relevant to the review. Given the rapidly evolving nature of cancer drug therapy, there are often several other trials that provide evidence indirectly relevant to the review. Important questions to be addressed by the Clinical Guidance Panel include: Would the use of this drug for the proposed indication improve the lives of cancer patients? Would their cure rates increase? Would they live longer? Would the growth of their cancers be better contained? Would their quality of life be better? Would their treatment-related side effects be acceptable? Which patients should be treated with this therapy, and which should not? Is there an alternative therapy that could be considered? How do these alternatives compare? All of that evidence has to be taken into the Canadian context when addressing the question of whether the drug under review represents an advance for cancer patients.

The task of evaluating the effectiveness of the treatment is made easier when the evidence includes one or more large, well-conducted randomized controlled trials with unequivocal results. However, the evidence often has gaps, or the quality of the evidence is low. The evaluation task is informed by the important input of the patients, registered clinicians, and PAG participating in the pCODR process.

Members of the Clinical Guidance Panel also interact with the Economic Guidance Panel to provide their clinical perspectives concerning the analysis of the cost-effectiveness of the treatment, often in the face of imperfect evidence and ever-changing practices that can vary between provinces and around the world. Input from the Clinical Guidance Panel can have a substantial effect on how the cost-effectiveness analysis is conducted, and that influence can in turn affect the recommendations made by the PERC about the cost-effectiveness of the treatment and the price negotiations that might subsequently ensue between drug manufacturers and payers.

Drawing on the reports from the Clinical and Economic Guidance panels, including all key stakeholder inputs, PERC formulates an initial recommendation.

The PERC has up to 16 voting members, including 3 patient members. Professional members of PERC are drawn from the fields of medicine, pharmacy, pharmacology, ethics, and health economics. Patient members are selected because of their personal knowledge of, experience with, and understanding of issues related to cancer and its management, among other qualifications[5].

The mandate of the PERC is to provide cancer drug funding recommendations, including conditions or criteria for coverage to the participating jurisdictions. Because the PERC meets each month, collegiality and unfettered open dialogue are fostered among the members. As part of the discussion, PERC draws on clinical information, including an assessment of the generalizability of the evidence to support a clear understanding of how the Clinical Guidance Panel came to its conclusions, and the strength of the evidence informing those conclusions, as well as considerations of epidemiology, patient perspectives, health economics, and implementation. The Clinical Guidance Panel and the Economic Guidance Panel leads are usually present at the meeting to provide additional support to PERC. In its deliberations before making a recommendation, PERC applies a deliberative framework (Figure 2) that considers the overall clinical benefit of the drug, patient-based values, cost-effectiveness, and adoption feasibility[6]. The application of the deliberative framework is critical to ensuring the consistency and transparency of PERC's recommendations.

FIGURE 2 The deliberative framework used by the pan-Canadian Oncology Drug Review's Expert Review Committee.

There are three categories of recommendations issued by pERC:

- A positive recommendation to reimburse the drug
- A conditional recommendation to consider reimbursing the drug only if certain conditions are met (for example, depending on better pricing of the drug)
- A negative recommendation not to reimburse the drug under review

An important element of the process is that all stakeholders (registered patient groups, registered clinicians, the submitter, the pAG) that contributed at the start of the process for a specific drug or indication are invited to provide feedback on the initial recommendation before the final recommendation is issued.

Once pERC issues a final recommendation on a particular drug, the pan-Canadian Pharmaceutical Alliance supports jurisdictions with joint negotiations to ensure value for publicly funded drug programs[7]. Although the pan-Canadian Pharmaceutical Alliance is separate from the pCODR process, its work builds on the review conducted by pCODR. Each participating jurisdiction then has to decide individually whether it will fund the particular drug.

The final funding decision is not taken lightly, and participating jurisdictions must consider several factors aside from pERC's recommendation, including its own budget, regional health system priorities, and local priorities. In keeping with pCODR's principle of transparency, the guidance reports (that is, the initial and final clinical and economic reports), initial and final recommendations, the reasons why the recommendation has been made, feedback from eligible participants, conflict of interest declarations, and funding decisions are published on the CADTH Web site for patients, clinicians, and others to view[8].

Since its implementation in July 2011 and up to 31 December 2016, the pCODR program has issued 80 notifications to implement (meaning a full and final recommendation). Of those 80 notifications, 9 were positive recommendations, 53 were conditional recommendations, and 18 were negative recommendations. More than 75% of the 62 positive and conditional recommendations have received uptake from one or more participating jurisdictions.

The pCODR program continues to evolve, and it strives to improve the process to engage all possible stakeholders. Clinician input and participation in the cancer drug approval process provide a way for clinicians to be part of the system, affecting funding decisions that could enhance patient outcomes for Canadians. Clinician engagement contributes to shaping the availability of cancer drugs based on clinical evidence, shared experiences, and a deep knowledge and understanding of patient needs.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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