Identification of Gaps and Opportunities for Provincial Reimbursement of Oncology Companion Diagnostics in Canada

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INTRODUCTION

Companion diagnostics (CDx) are medical devices used to measure an individual's protein expression, gene expression, or detect genetic variations, for the safe and effective use of a corresponding drug or biological product. It aims to match therapeutic products to those patients who will positively respond to that therapeutic product, to maximize benefits and minimize risks from the therapeutic products received.[1] CDx can be classified as either in-vitro diagnostic devices (IVDDs) or laboratory developed tests (LDTs). LDTs enter the
Canadian market without formal regulatory review and are the most common type of CDx in Canada.[2] For the purposes of this analysis, a diagnostic will be considered a CDx if it is required prior to the provision of a targeted therapy.

CDx tests or assays are specifically developed for use as a companion to a particular drug therapy. The value of these instruments are to support the choice of drug therapy through identification of patient subtypes and/or genetic alterations for healthcare providers. In identifying an appropriate patient population, targeted treatments can ultimately improve health outcomes and avoid adverse drug reactions.

In Canada, oncology drugs, IVDDs and LDTs enter the healthcare system through pathways with little formal coordination between the processes. This lack of formal coordination presents a challenge to the current organization of the healthcare system, as decisions on which drugs, medical devices and laboratory tests to provide for patients are made by different decision-makers. This can create a great deal of inconsistency and a heterogeneous landscape throughout Canada for patients accessing companion diagnostics. Consequently, patients may have their treatment options and outcomes impacted.

In 2017, the Canadian Agency for Drugs and Technologies in Health (CADTH) incorporated CDx within its drug review process to inform considerations for implementation of the associated therapy. However, no formal funding recommendation for the CDx is provided through this Health Technology Assessment (HTA).[3]

Rather, funding decisions are made provincially with minimal transparency. This research aims to identify where in the reimbursement pathway of CADTH-participating provinces do gaps exist in patient access to oncology therapeutics and the associated CDx.

METHODS

All publicly available pan-Canadian Oncology Drug Review (pCODR) appraisal reports, funding recommendations and provincial funding summaries between January 1st 2019 and March 25th 2021 were identified, as well as completed health technology assessments (HTA) by CADTH-participating provinces with an HTA process for devices (British Columbia, Alberta, Ontario).

Extracted information included therapeutics, targeted biomarker, CDx, funding status of the therapeutic and CDx, and dates of final recommendations and provincial funding. Extracted pCODR reviews included oncology drugs, both that reported a CDx and those where no CDx was reported. Extracted provincial HTA reviews included only CDx technology; gene expression profiling tests were excluded because they were not associated with screening requirements for specific drugs. Statistical comparisons between pCODR reviews that reported a CDx versus those that did not report a CDx were performed using a two-tailed Mann-Whitney U test; the data was visualized and found to not be normally distributed.

RESULTS

50 pCODR reviews with a final recommendation were identified, of which 22(44%) reviews reported requiring a CDx to identify appropriateness of therapy. Of these, 17(77%) reviews requiring a CDx had the CDx funded, and 5(23%) reviews requiring a CDx did not have the CDx funded (Figure 1).

Of the reviews where the CDx is funded, 3(18%) of the associated oncology drugs reviewed by CADTH were funded in at least 5 provinces. Of the reviews where the CDx is not funded, 3(60%) of the associated oncology drugs reviewed by CADTH were funded by at least 5 provinces.

CDx that are funded included testing for the following biomarkers: CD30, CD33, KIT D816V, HER2, ER/PR, BRCA, EGFR, PD-L1 and Ph+. The CDx that are not funded include testing for NTRK gene fusion, IDH2/NGS, PD-L1, ROS1 and BRAF. Sometimes, as in the case for testing of PD-L1, the CDx is funded only for a specific indication. CDx that are funded were already the standard of care (SoC) for that disease space or indication. CDx that are not funded were not routinely available to patients either in general, or for their specific indication.

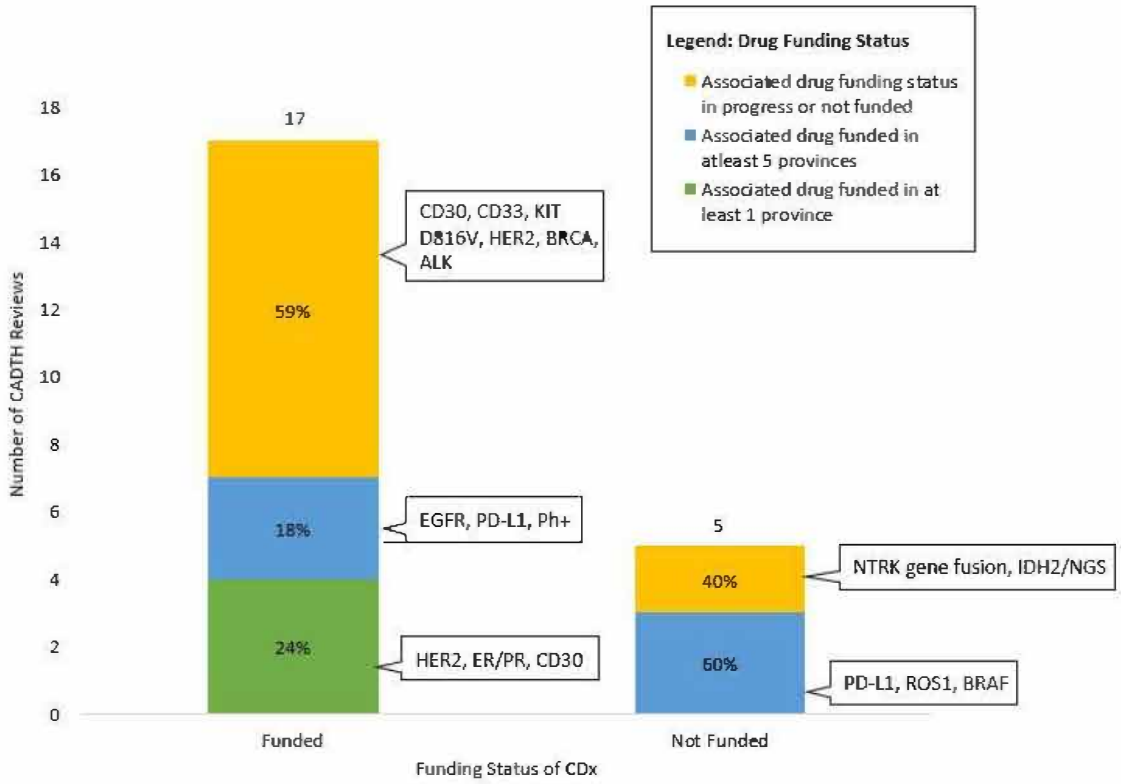


Figure 1. Provincial funding status of oncology drugs reviewed by CADTH requiring a CDx

Abbreviations: BRCA – Breast CAncer gene; EGFR – Estimated glomerular filtration rate; ER – Estrogen receptor; HER2 – Human epidermal growth factor receptor 2; IDH2 - Isocitrate Dehydrogenase; KIT D816V; NGS – Next generation sequencing; NTRK - Neurotrophic tropomyosin receptor kinase; PD-L1 - Programmed death-ligand 1; Ph+ - Philadelphia chromosome positive; PR – Progesterone receptor

Of the reviews requiring a CDx, where the CDx is funded, 12(71%) of the drugs reviewed by CADTH received a positive recommendation (Figure 2). In addition, of the reviews requiring a CDx, where the CDx is not funded, 2(40%) of the drugs reviewed by CADTH received a positive recommendation.

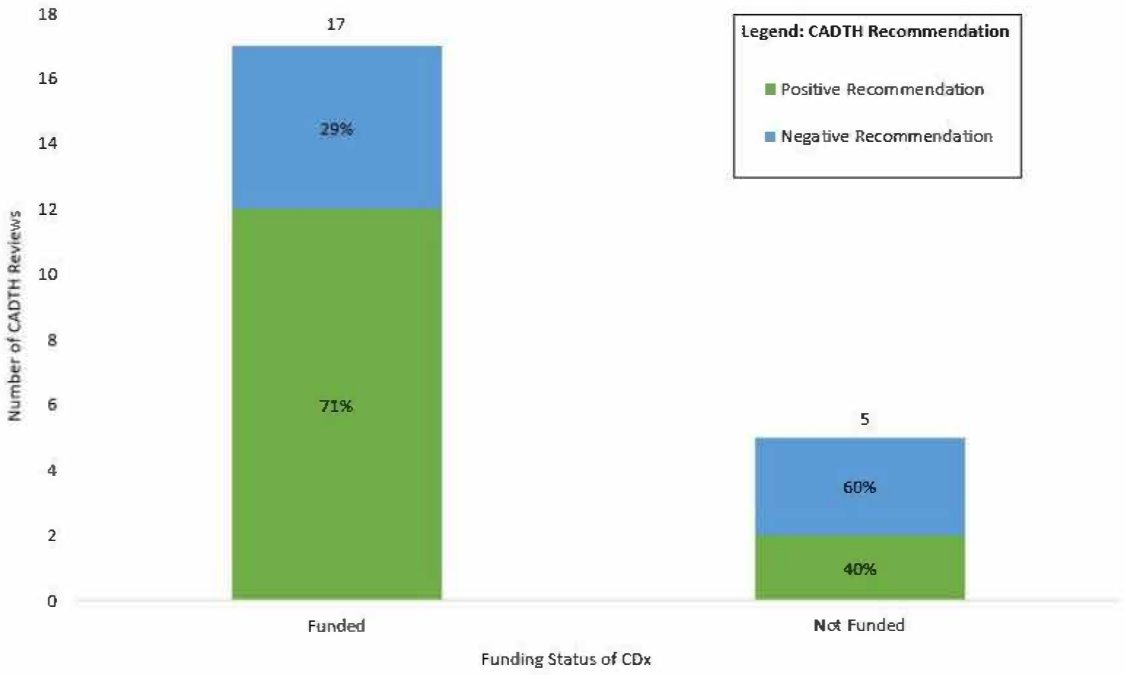


Figure 2. Final recommendations of oncology drugs reviewed by CADTH requiring a CDx

RESULTS

CDx may be reviewed by the CADTH Optimal Use pathway, INESSS, and at the provincial-level by CADTH-participating provinces, as displayed by the infographic in Figure 3.

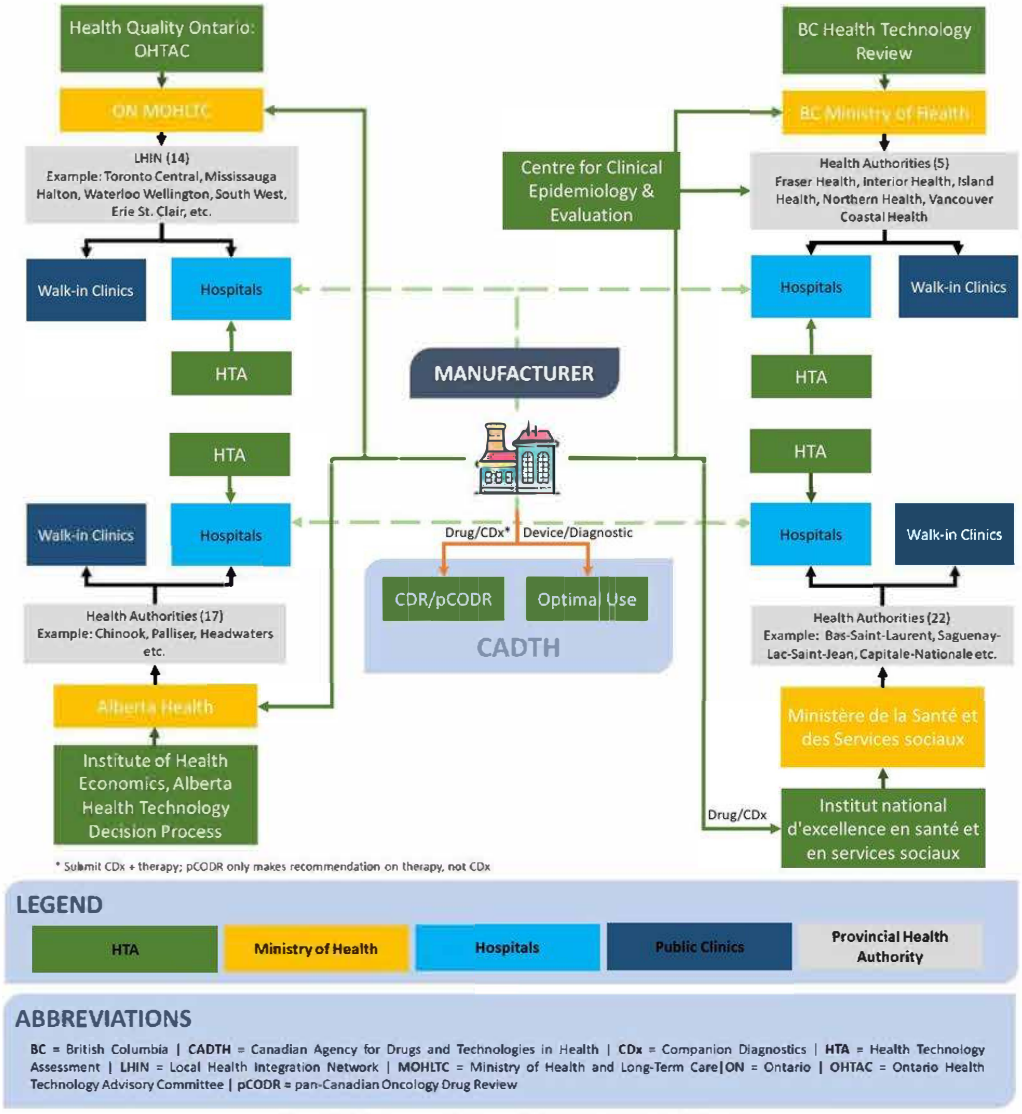


Figure 3. Reimbursement pathway for health technologies in Canada

Since its initiation, Health Quality Ontario completed 12 HTA reviews relating to cancer, of which 1 was a genetic test for EGFR mutation. Alberta completed 33 HTA reviews, of which 3 related to cancer but none contained a CDx. British Columbia completed 18 HTA reviews, of which 2 related to cancer but neither contained a CDx (Figure 4).

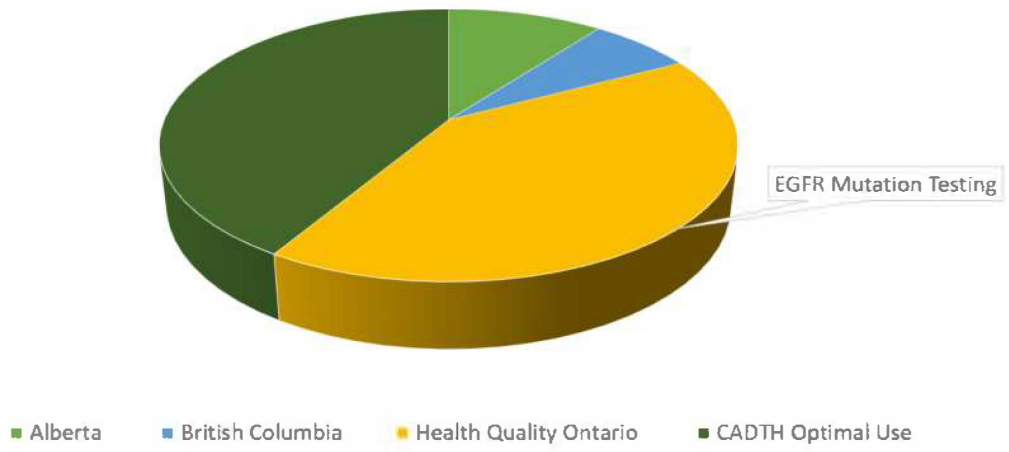


Figure 4. Oncology technology reviews by CADTH-participating provinces

No significant difference (p = 0.1902) was found in the number of days to provincial funding of a drug, after a final CADTH recommendation was issued, between reviews that report a CDx versus those that did not report a CDx (Figure 5).

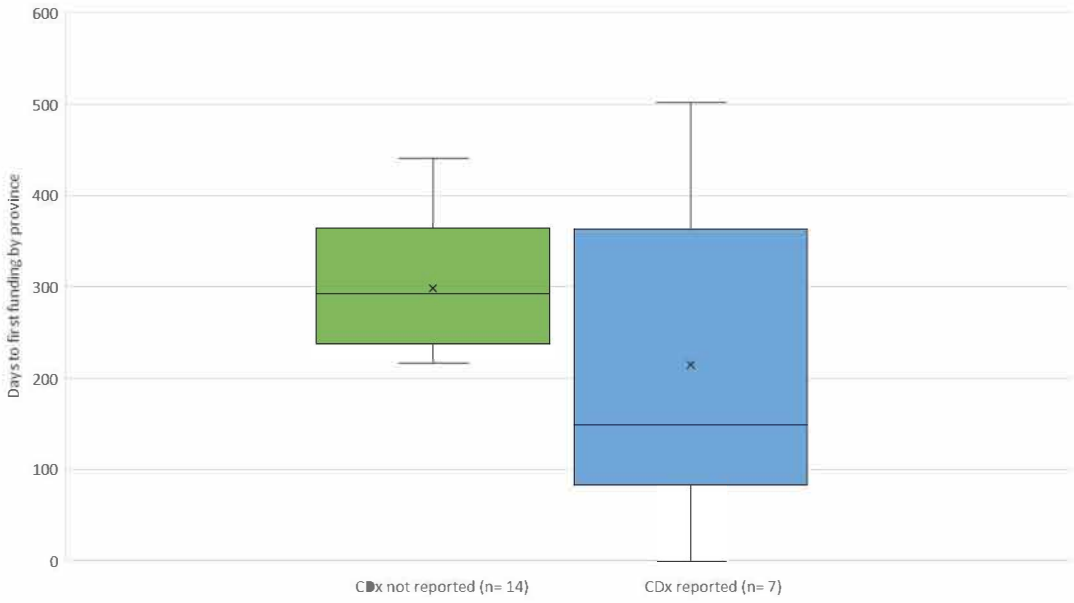
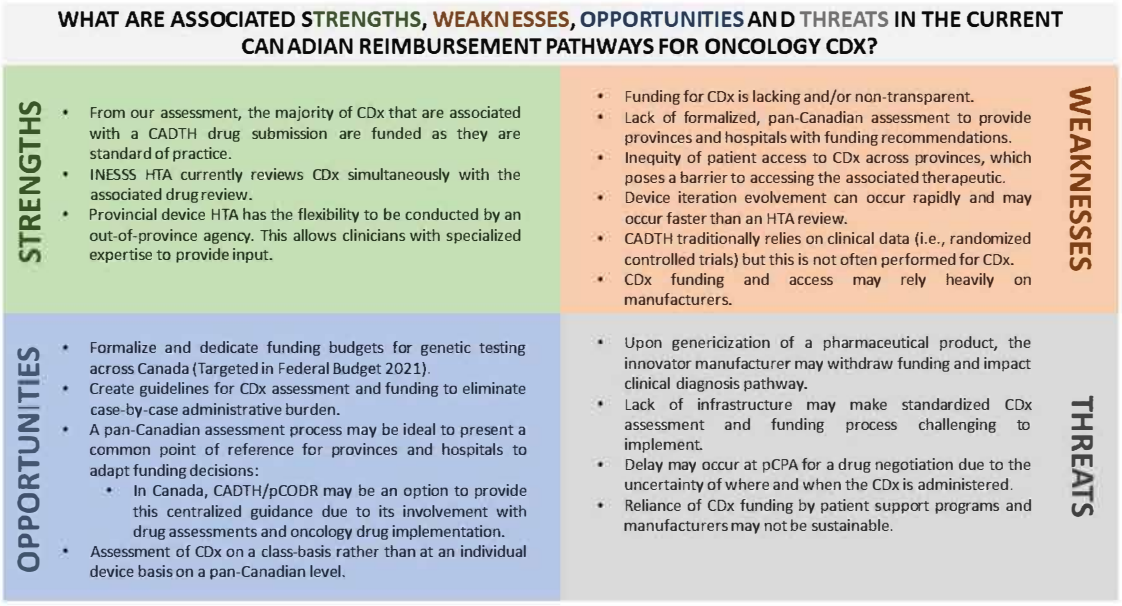


Figure 5. Quantifying delays in provincial funding of oncology drugs for pCODR reviews with and without a CDx

DISCUSSION



SWOT analysis based on the results, as well as from literature and stakeholder input revealed no formalized funding for CDx results in individual hospitals evaluating/offering genetic tests, or pharmaceutical manufacturers covering CDx cost. Although a majority of identified CDx are currently funded as part of SoC, there exists gaps in assessment of novel CDx. There exists opportunities to implement a formalized assessment process for CDx on a pan-Canadian level to provide a common point of reference for provinces and hospitals when making funding decisions. Though CADTH may require additional infrastructure and expertise, it could be leveraged to provide guidance on funding due to its present role in oncology drug implementation recommendations. Standardized funding and assessment processes are key to ensuring equitable access to healthcare for all patients.

Future studies should explore the funding status of not only manufacturer-submitted CDx, but also diagnostics that may not directly be associated with a specific drug, such as tests that evaluate protein levels in order to direct patients to the right treatment pathway or a genetic testing panel. This research could supplement the guidance for the lack of coordination and standardization of funding for health technology and diagnostics.

LIMITATIONS & CONCLUSION

There are limitations that exist within this study. One limitation is the small sample size of pCODR reviews identified after January 1st, 2019. The sample of reviews collected are representative of pCODR reviews with a final recommendation, in order to understand the implications of provincial funding following a recommendation. Another limitation is possibly the most up to date funding status of oncology drugs and the associated CDx, as the authors solely based this information off CADTH provincial funding summaries and clinical guidance reports. In addition, HTA assessments by participating provinces (i.e., British Columbia, Alberta, and Ontario) were included in this analysis, however there are a number of provinces with a less centralized procedure to evaluate health technology, which limits the ability to capture HTA reviews across all provinces. A final limitation is a lack of transparency around manufacturer-funded CDx, resulting in an unclear understanding of the conditions involved in patients qualifying for access to the test and by extension, the specific drug.

Despite CADTH guidelines for therapeutics requiring a CDx, reimbursement gaps exist between jurisdictions where an oncology drug is funded but the associated CDx is not. This calls for a coordinated CDx review process that includes guidance and funding recommendations from a central body, in order to ensure equitable patient access to targeted oncology care.

DISCLOSURES

The authors declare that they have no conflict of interest.

ABSTRACT

Objectives: Companion diagnostics (CDx) are administered prior to treatment with a therapeutic. Within oncology, CDx detect single biomarkers or genes. The Canadian Agency for Drugs and Technologies in Health (CADTH) review process incorporates CDx, with guidance on inclusion in economic evaluations for therapeutics, though does not provide funding recommendations. Funding decisions for genetic tests are made provincially. This research aims to identify where in the reimbursement pathway of CADTH-participating provinces do gaps exist in patient access to oncology therapeutics and the associated CDx.

Methods: All publicly available pan-Canadian Oncology Drug Review (pCODR) appraisal reports, funding recommendations and provincial funding summaries after January 1st 2019 were identified, as well as completed health technology assessments (HTA) by CADTH-participating provinces with HTA processes for devices (British Columbia, Alberta, Ontario). Extracted information included therapeutics, targeted biomarker, CDx, funding status of the therapeutic and CDx, and final recommendations.

Results: 22 pCODR reviews reported requiring a CDx, of which 5(23%) reported a CDx that was not funded as standard of care. Of these, 3(60%) drugs were funded by at least 5 provinces. Health Quality Ontario completed 12 HTA reviews related to cancer, of which 1 was a genetic test for EGFR mutation. Alberta and BC completed 33 and 18 HTA reviews, respectively, of which none were for oncology CDx. SWOT analysis from literature and stakeholder input revealed no formalized funding for CDx results in individual hospitals evaluating/offering genetic tests, or pharmaceutical manufacturers covering CDx cost. These approaches result in inequitable access across patient groups and pose challenges to implementation.

Conclusion: Despite CADTH guidelines for therapeutics requiring CDx, reimbursement gaps exist between jurisdictions where an oncology drug is funded but the associated CDx is not. This calls for a coordinated CDx review process that includes guidance and funding recommendations from CADTH, ensuring equitable patient access to targeted oncology care.

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