Access to Drugs for Cancer

Does Where You Live Matter?

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ABSTRACT

Background: Provincial governments are responsible for administering publicly-funded anti-cancer drug benefit programs in Canada. This study examines inter-provincial variations in not only the content of such programs, but also the policies/processes used when considering a new drug for coverage.

Methods: Pharmaceutical manufacturers and provincial /regional cancer boards were surveyed to identify the drugs covered by public drug benefit plans. Kappa coefficients were calculated to determine inter-provincial coverage variations. The comprehensiveness of availability of anti-cancer drugs across the country was also assessed. A semi-structured survey of all 10 provincial/regional cancer board pharmacy and therapeutics (P&T) committees was employed to examine decision-making policies/procedures. It included questions on committee composition and processes and on factors influencing decisions regarding the introduction of new drugs. Completed surveys were analyzed using qualitative and quantitative techniques.

Results: All cancer boards and 75% of manufacturers contacted provided information on drugs covered in each province. Where lists were obtained from both sources, there was full agreement on content. Kappa values calculated ranged from -0.403 to 0.594, indicating poor to moderate agreement on anti-cancer drug coverage between provinces. Only 7 of the 115 drugs were available in all 10 provinces. Regarding decision-making processes, while ratings for both the relative importance and use of factors involved in decision-making (clinical effectiveness, patient preference, etc.) were similar across provinces, those for the relative importance and use of different information types (clinical trials, expert opinion, etc.) varied.

Conclusion: Access to anti-cancer drugs clearly varies across the country. In part, this may be due to differences in the views of P&T committees on the usefulness of information they use in their deliberations.

MeSH Terms: Formularies; antineoplastic agents; Canada; decision-making

La traduction du résumé se trouve à la fin de l'article.

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In Canada, there are a number of different "payers" for drugs provided through out-patient programs (i.e., where patients visit a health care facility for treatment without spending the night), which do not fall within the domain of the Canada Health Act. They may be broadly categorized into three groups: 1) government programs (e.g., drug formularies), 2) employer-sponsored benefit packages, and 3) "out-of-pocket" payment. This paper focusses on the first of these three (i.e., the publicly-funded programs). Government benefit programs are typically administered by individual provinces, each of which independently makes decisions around what drugs to provide and to whom based upon the recommendations of a local pharmacy and therapeutics (P & T) committee. Consequently, patient eligibility criteria, as well as the content and scope of the formularies (i.e., list of publicly covered drugs), themselves, vary among provinces, creating a level of inequity in nation-wide access to drugs that could ultimately lead to regional disparities in the health of the Canadian public as a whole.

To date, research examining formulary decision-making and the comparative comprehensiveness of publicly-funded drug coverage across provinces has been limited to analyses of eligibility, cost-sharing arrangements, drug expenditures, and access to out-patient drugs for qualifying sub-populations (e.g., seniors, children, or those receiving social assistance),¹⁻⁵ none of which have included drugs for treating cancer. Such drugs play a critical role in the management of many types of cancer, often comprising patients' only therapeutic option. In recent years, the development of high-cost, innovative anti-cancer drugs that offer new hope for improved survival and/or quality of life has significantly increased, placing pressure on provincial cancer boards/agencies and their P&T committees to make them available to patients. It has also resulted in a need to examine current access to these drugs in Canada, with questions such as "Does where you live matter?" likely to be raised more and more frequently. Thus, this study aims to 1) identify variations in the availability of publicly-funded anti-cancer drugs across Canada, and 2) examine factors that may be contributing to any potential variations observed.

TABLE I

Kappa Scores Indicating Level of Agreement on the Availability of Anti-cancer Drugs to All Cancer Patients

Province	A	B	C	D	E	F	G	H	I	J
A	X	0.455	0.438	0.271	0.594	0.033	0.142	0.280	0.323	0.341
B	X	X	0.498	0.497	0.319	0.026	0.141	0.332	0.401	0.371
C	X	X	X	0.572	0.476	0.040	0.144	0.361	0.344	0.362
D	X	X	X	X	0.335	0.104	0.145	0.306	0.433	0.324
E	X	X	X	X	X	0.067	0.072	0.460	0.395	0.414
F	X	X	X	X	X	X	-0.403	0.211	0.104	0.151
G	X	X	X	X	X	X	X	0.027	0.023	-0.002
H	X	X	X	X	X	X	X	X	0.306	0.371
I	X	X	X	X	X	X	X	X	X	0.388
J	X	X	X	X	X	X	X	X	X	X

METHODS

Data collection

Part I: Identification of Variations in Anti-cancer Drug Availability

A list of all new anti-cancer molecules (classified as antineoplastics, immunomodulating agents, biological response modifiers, hormones or substitutes, or unclassified therapeutic agents under the Anatomical, Therapeutic and Chemical Classification scheme⁶) approved for sale in Canada between 1 January 1991 and January 2003, along with their manufacturers, was compiled using Health Canada's Notice of Compliance for Drug Products Database.⁷ A total of 115 drugs, produced by 20 manufacturers, were identified. Given the purpose of the study (i.e., to assess the availability of cancer drugs in each province from a policy perspective as opposed to a clinical one) and the level of data available from public sources, these drugs were not grouped according to cancer type.

Manufacturers and cancer boards/agencies were then surveyed to determine the availability of these drugs within existing publicly-funded provincial cancer programs. For each province, manufacturers were asked to identify which of their drugs was part of the formulary and state any conditions on its use (e.g., type and/or cancer stage). At the same time, copies of published anti-cancer drug benefit plans from provincial cancer boards/agencies were obtained. In provinces where such a document was not available, a list of all drugs appearing on at least one of the published plans was compiled and sent to pharmacy managers/directors, each of whom was asked to 1) indicate the drugs currently offered to patients meeting relevant clinical criteria, and 2) provide the names of any other drug(s) not appearing

TABLE II

Comprehensiveness of Anti-cancer Drug Coverage Across Provinces

Number of Provinces Providing Coverage	Number of Drugs	Percentage of Drugs
1	5	4.3%
2	2	1.7%
3	5	4.3%
4	8	7.0%
5	7	6.1%
6	7	6.1%
7	13	11.3%
8	13	11.3%
9	48	42.0%
10	7	6.1%
Total	115	100%

on the list. Since in some provinces, certain anti-cancer drugs (e.g., oral forms) are accessed through a general government drug benefit plan rather than a specific cancer board/agency program, benefit lists for these plans were collected as well.

Part II: Factors Contributing to Potential Variations in Anti-cancer Drug Access

The Chief Executive Officer, the Chair of the P&T Committee, and the pharmacy manager/director in each of the 10 provincial/regional cancer boards/agencies were sent semi-structured, self-administered questionnaires that they were asked to complete independently. The questionnaire contained 2 sections, the first of which included questions about: P&T Committee composition and its operational structure, the number and professional mix of members, meeting frequency, whether "ad hoc" or "as needed" meetings are held, timing of benefit list updates, use of standard processes/guidelines during decision-making, appeals mechanisms, availability/transparency of rationale for decisions to stakeholders, and approaches to communicating Committee decisions. The second section addressed specific factors hypothesized as potentially influencing decision-making. It consisted of 2 sets of Likert-type questions, one focussing on the importance of various *types* of information

to P&T Committees (e.g., pharmacologic profile, quality of clinical evidence, and status of existing comparator therapies), and the other focussing on *sources* of information and their importance to P&T Committees (e.g., published literature expert opinion, and manufacturer's promotional literature). The 5-point Likert scale ranged from 1 ("this factor is not important at all") to 5 ("this factor is extremely important").

Data analysis

Part I: Identification of Variations in Anti-cancer Drug Availability

Anti-cancer drug lists from cancer boards/agencies and manufacturers were compared for consistency. Upon resolving discrepancies through contact with relevant cancer agencies/boards, 4 coverage lists for each province, which varied by patient type, were created: 1) all cancer patients, 2) those on social assistance, 3) nursing home residents, and 4) seniors (age ≥ 65 years).

Agreement on the content of all 4 anti-cancer drug coverage lists between pairs of provinces was assessed using the Kappa statistic. It measures level of agreement beyond chance between two sets of observations (e.g., two lists of "covered" drugs). Kappa values range from -1 to 1, with "strength of agreement" interpreted as follows:⁸ $K > 0.75$ = excellent agreement,

TABLE III

Extent to Which Ratings on the Importance of Information Types to Anti-cancer Drug Coverage Decision-making Varied Across Provinces

Information Type	Mean Importance Rating (SD)*	Median Importance Rating*	Range of Importance Ratings*
Pharmacologic profile	4.5 (0.53)	4.5	4-5
Quality of relevant clinical evidence	4.5 (0.53)	4.5	4-5
Availability of and comparability with existing therapies	4.3 (0.48)	4.0	4-5
Potential therapeutic impact	4.2 (0.42)	4.0	3-5
Budgetary impact	4.0 (0.82)	4.0	3-5
Patient preferences	3.2 (0.79)	3.0	2-5

* Based on all 10 responses received

Note: 1 = not important; 2 = slightly important; 3 = somewhat important; 4 = very important; 5 = extremely important

TABLE IV

Extent to Which Ratings on the Importance of Information Sources to Anti-cancer Drug Coverage Decision-making Varied Across Provinces

Information Source	Mean Importance Rating (SD)*	Median Importance Rating*	Range of Importance Ratings*
Clinical efficacy trials	4.2 (1.23)	4.5	1-5
Prospective effectiveness studies	4.2 (1.23)	4.5	2-5
Requesting physician justification	3.8 (0.42)	4.0	3-4
Literature syntheses	3.6 (1.17)	3.5	2-5
Pharmacoeconomic studies	3.5 (1.18)	3.0	2-5
Quality-of-life assessments	3.3 (0.94)	3.0	2-5
Retrospective studies	3.0 (0.94)	3.0	2-5
Expert opinion	3.0 (0.94)	3.0	2-5
Other provincial formularies	3.0 (1.05)	3.0	1-4
Government reports	2.1 (0.88)	2.0	1-3
Promotional literature	1.8 (0.92)	1.5	1-3
Testimonials	1.2 (0.42)	1.0	1-2

* Based on all 10 responses received

Note: 1 = not important; 2 = slightly important; 3 = somewhat important; 4 = very important; 5 = extremely important

$0.40 \leq K \leq 0.75$ = fair to good agreement, and $K < 0.40$ = poor agreement.

Part II: Factors Contributing to Potential Variations in Anti-cancer Drug Access

Responses from questionnaires were analyzed in two ways. Qualitative methods, based on content analysis, were used to aggregate, synthesize and interpret answers to open-ended questions. This involved extracting, classifying, and coding information "chunks" by two independent researchers. Analyses of answers to Likert-type questions employed standard quantitative (statistical) techniques, and included calculation of the mean, median, standard deviation and range of values for each response.

RESULTS

Part I

Although 15 of the 20 pharmaceutical companies (75%) surveyed responded, only about half completed the entire question-

naire, indicating that such information was not readily available. All 10 cancer agencies responded, of which 4 provided copies of their benefit lists while the remaining 6 checked off drugs covered on the list that accompanied the questionnaire. Where data from both manufacturers and cancer agencies were obtained, full agreement on coverage information was found.

Kappa scores, demonstrating the level of agreement between each pair of provinces in drug lists applicable to all cancer patients are presented in Table I. Rows and columns indicate the provinces, anonymized to comply with conditions under which ethics approval for the study was received. Scores ranged from -0.403 to 0.594 (mean value of 0.266 (standard deviation (SD) 0.165)), indicating poor to fair agreement, at best. Those for the three subgroups were similar to values obtained for the full group of cancer patients: social assistance recipients: mean $K=0.307$ (SD 0.233); nursing home residents: mean $K=0.301$ (SD 0.234); and seniors: mean $K=0.300$ (SD 0.236).

Table II demonstrates the comprehensiveness of coverage of drugs across the provinces. Only 7 drugs were found to be covered by all provinces, and 5 appeared to be available in only one of the provinces (not consistently the same one).

Part II

One completed questionnaire was received from each jurisdiction. Participants included 1 CEO, 1 physician, and 8 managers/directors of pharmacy departments. According to the responses received, the number of members on P&T committees ranged from 12 to 28, and professional mix varied. Physicians constituted 31-60%, and in half of the jurisdictions, they comprised at least 50% of the membership. Between 17-25% were pharmacists, and 6-30% were administrators. In some jurisdictions, the committee included lawyers and community representatives.

Differences in committee processes were also observed. The frequency of "regular" meetings and updates to benefit lists varied. Some jurisdictions held "ad hoc" meetings. Two jurisdictions reported not using standard processes in decision-making. Finally, all but one jurisdiction reported using different processes for different categories of drugs being considered (e.g., "breakthrough" drugs vs. "line extensions").

The extent to which various *types* of information were viewed as important to P&T committees is summarized in Table III. All committees rated "pharmacologic profile", "quality of relevant clinical evidence", and "availability of and comparability with existing therapies" as being either "very important" or "extremely important". In contrast, the importance of "budgetary impact" and "patient preference" varied considerably across provinces. The importance of different *sources* of information is shown in Table IV. Clinical efficacy trials and testimonials were consistently rated by provinces (with one exception) as extremely important and not important, respectively. However, there was far less agreement on the importance of literature syntheses, pharmacoeconomic analyses and expert opinion. Table V shows how often the various sources of information were *actually used* (since use depends, in part, on availability). It differs from Table IV in

that it provides information on the actual use of certain types of information, as opposed to what has been deemed important but may rarely be used. While frequent use of clinical efficacy trials and marginal use of testimonials were noted in all provinces, rates for literature syntheses and expert opinion varied.

DISCUSSION

Previous research has demonstrated that prescription drug coverage varies across provinces^{4,5}. However, until now, little was known about whether such variations existed for anti-cancer drugs.

According to the results of this study, there appears to be minimal agreement (after adjusting for chance) in the lists of publicly-funded anti-cancer drugs between any two provinces, demonstrating that where you live does seem to matter. Analyses of patient subgroups (separately involving those on social assistance, in nursing homes, or ≥ 65 years) produced similar findings. This may be explained by the fact that anti-cancer drugs are typically accessed through a provincial or hospital-based program which covers all patients, regardless of their age or socioeconomic status. With respect to benefit program comprehensiveness across provinces, 7 of the 115 anti-cancer drugs examined appeared on all 10 provincial plans, while 5 were found on only 1. Nearly half of the drugs were listed by at least 9 of the 10 provinces. Although it could be argued that more is not necessarily better, the presence of each of the 115 drugs on at least 1 of the 10 formularies indicates that a minimum of 1 provincial board/agency considered the drug important enough to provide to patients within its jurisdiction. Therefore, these findings also suggest that location of residence (on a provincial level) may affect patient access to certain new and innovative anti-cancer drugs.

The findings from this study mirror those from a project recently completed by the National Cancer Director of the National Health Service in the United Kingdom.⁹ Variations in the use of 16 cancer drugs across the country were examined using data from IMS Health and the 34 cancer networks in England. The data included aggregated information

TABLE V

Extent to Which Ratings on the Use of Different Information Sources in Anti-cancer Drug Coverage Decision-making Varied Across Provinces

Information Source	Mean Utilization Rating (SD)*	Median Utilization Rating*	Range of Utilization Ratings*
Clinical efficacy trials	3.9 (0.32)	4.0	3-4
Requesting physician justification	3.9 (0.32)	4.0	3-4
Prospective effectiveness trials	3.3 (1.1)	4.0	1-4
Literature syntheses	3.1 (0.88)	3.0	2-4
Pharmacoeconomic studies	2.9 (0.88)	3.0	2-4
Expert opinion	2.9 (0.74)	3.0	2-4
Other provincial formularies	2.7 (0.95)	3.0	1-4
Quality-of-life assessments	2.4 (0.71)	2.0	2-4
Retrospective studies	2.4 (0.70)	2.0	2-4
Government reports	1.8 (0.63)	2.0	1-3
Promotional literature	1.5 (0.71)	1.0	1-3
Testimonials	1.1 (0.32)	1.0	1-2

* Based on all 10 responses received

Note: 1 = never; 2 = occasionally; 3 = often; 4 = always

(i.e., not stratified by cancer drug or type) on drugs prescribed and administered in hospital settings. After adjusting for casemix differences, 2.6 to 11.6 fold variations in drug usage across networks were observed.

As outlined in the Methods section, questionnaires were sent to 3 individuals in each of the 10 provinces in an attempt to collect 3 different perspectives on information-related factors that affect coverage decisions. It was thought that such information would be helpful in determining whether or not CEOs, P&T chairs (typically clinicians treating cancer patients) and managers/directors viewed the importance of these factors differently. Further, it would serve as a means through which responses received could be validated. In the end, only one completed questionnaire was returned from each jurisdiction. Nevertheless, based upon the information collected through these questionnaires, it was still possible to reach several conclusions. P&T committees are different, not only in their composition (i.e., types of individuals on the committee), but also in the way that they make decisions (e.g., how information is prepared, presented, and valued). Further, the importance and actual use of certain types of information (e.g., literature syntheses, pharmacoeconomic evaluations and quality-of-life studies) varies across committees. Such variations may be contributing to the observed inter-provincial differences in anti-cancer drug benefit lists.

Since the clinical care of cancer patients depends in part upon whether or not certain treatment options are covered through provincial cancer board/agency drug bene-

fit programs, it becomes important to find ways of equalizing access to anti-cancer drugs across the country. Last year, Canada launched its Common Drug Review (CDR). In this process, pharmaceutical manufacturers submit their application for inclusion of a new drug on provincial formularies to a national review committee, which, in turn, makes a single listing recommendation. The individual provinces are then free to decide whether or not to accept the recommendation. While it is still too early to assess the impact of the CDR on access to anti-cancer drugs, it is anticipated that such a centralized review mechanism will lead to more consistent formulary decision-making across provinces.

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RÉSUMÉ

Contexte : Au Canada, l'administration des programmes publics de remboursement du prix des médicaments contre le cancer incombe aux gouvernements provinciaux. Nous avons voulu étudier les écarts entre les provinces, non seulement du point de vue du contenu de ces programmes, mais des politiques et processus utilisés lorsqu'on envisage l'ajout d'un nouveau médicament remboursable.

Méthode : Nous avons sondé des sociétés pharmaceutiques et des offices provinciaux ou régionaux du cancer afin de dresser la liste des médicaments assurés par les régimes publics, puis calculé les coefficients Kappa pour déterminer l'agrément entre les provinces à cet égard. Nous avons aussi évalué l'intégralité des médicaments anticancéreux assurés selon le lieu. Un questionnaire semi-structuré administré aux comités pharmaceutiques et thérapeutiques des 10 offices provinciaux ou régionaux du cancer a permis d'examiner les politiques et procédures décisionnelles. Certaines questions portaient sur la composition et les processus des comités, et d'autres, sur les facteurs influençant les décisions d'assurer ou non de nouveaux médicaments. Les réponses aux questionnaires ont été analysées à l'aide de techniques qualitatives et quantitatives.

Résultats : Tous les offices du cancer et 75 % des fabricants contactés ont fourni des renseignements sur les médicaments assurés dans chaque province. Lorsque les deux sources nous ont fourni des listes, celles-ci concordaient entièrement. Les valeurs Kappa calculées variaient de 0,403 à 0,594, ce qui montre un accord faible à modéré entre les provinces à l'égard des médicaments anticancéreux assurés. À peine 7 médicaments sur 115 étaient assurés dans toutes les provinces. En ce qui concerne les processus décisionnels, les résultats concernant l'importance relative des facteurs en cause dans la prise de décisions (efficacité clinique, préférences des patients, etc.) et les résultats sur l'utilisation de ces facteurs étaient semblables d'une province à l'autre, mais les résultats concernant l'importance relative et l'utilisation de différents types de données (essais cliniques, opinions d'experts, etc.) variaient.

Conclusion : Il est clair que l'accès aux médicaments anticancéreux varie d'un endroit à l'autre du pays. Cela s'expliquerait en partie par les différences dans les points de vue des comités pharmaceutiques et thérapeutiques quant à l'utilité des données qu'ils utilisent dans leurs délibérations.

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