

Interprovincial variation in access to publicly funded pharmaceuticals:

A review based on the WHO Anatomical Therapeutic Chemical classification system

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Introduction: Government-funded drug programs provide prescription medications for many Canadian residents, including senior citizens and social assistance recipients. Pharmaceuticals available for beneficiaries are typically listed in federal, provincial, and territorial formularies. We analyzed six Canadian drug formularies (for the provinces of Alberta, British Columbia, Manitoba, Nova Scotia, Ontario, and Quebec) and report the extent of interprovincial variation in Canadians' access to publicly funded pharmaceuticals at the chemical subgroup (CSG) level of the World Health Organization Anatomical Therapeutic Chemical (WHO ATC) classification system.

Methods: A database profiling provincial formulary listings of CSGs was compiled to enable a cross-sectional analysis of drug benefits at a clinically meaningful level. The comprehensiveness of provincial drug reimbursement plans was evaluated in a quantitative comparison of CSGs. Therapeutic distribution of CSGs within anatomical main groups of the

WHO ATC classification system was also investigated. Interprovincial formulary agreement of CSG listings (full, restricted, or not listed) was determined on the basis of kappa coefficients.

Results: British Columbia and Nova Scotia provided residents with access to the greatest number of full-listing CSGs, 336 each. Manitoba had the fewest full-listing CSGs, 268. Kappa coefficients, representing agreement in provincial listing decisions, ranged from 0.23 (between British Columbia and Quebec) to 0.45 (between Alberta and Manitoba). All of these coefficients represent a fair-to-poor level of interprovincial agreement in CSG listing status.

Conclusion: A large degree of variation is present in Canadian provincial drug formularies, even at the CSG level. This reflects differences in provincial listing decisions and has therapeutic implications for patients, in that there is differential access to entire categories of drug products across provincial drug plans.

Since its inception in 1967, "universality" has been one of the pillars of medicare under the Canada Health Act. In the past four decades, Canadians have increasingly relied on pharmaceuticals to help manage and prevent disease, avoid costly and invasive treatments, and improve overall quality of life. Changes in relative utilization of drugs have resulted in a significant public policy focus on our increased total spend on medications. The public sector funds 45% of total expenditures for retail prescription drugs in Canada,¹ primarily for senior citizens and social assistance recipients. The inability of these individuals to access medications may affect their own health and impede Canada's ability to improve the health of the population as a whole. It tends to undermine the pillar of universality in medicare.

Public funding is not available for all of the drugs approved for use in Canada. Medications that are available for reimbursement are typically identified in federal, provincial, and territorial drug formularies, although there may also be special drug programs providing coverage

through retail venues or the hospital sector. Provinces and territories may approve full access or place restrictions on the medications they include in the formulary, requiring patients to meet specific medical criteria before providing reimbursement. Alternatively, provinces and territories may decide not to list certain medications at all.

All new drug entities submitted for formulary listing in Canada are now evaluated through the Common Drug Review process, managed by the Canadian Coordinating Office for Health Technology Assessment (CCOHTA).² This process, formally implemented one year ago (September 2003), provides a single listing recommendation to all participating federal, provincial, and territorial drug plans.

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Study is first to compare complete formularies

▶ **See Commentary, page 14.**

However, the plans are not required to comply with the recommendation.

Previous comparisons of provincial formularies have shown considerable diversity in the listing of reimbursable medications in Canada.^{3,4} In contrast with those studies, which analyzed the formulary status of predetermined selections of medications, this investigation is the first involving a comparison of entire provincial formularies. This study also contributes new findings by examining pharmaceuticals at the chemical subgroup (CSG) level (see box), as defined by the World Health Organization (WHO).⁵ By way of example, Table 1 illustrates the WHO ATC coding system for one drug, rofecoxib.

WHO's classification system

The WHO Anatomical Therapeutic Chemical (ATC) classification system was selected for use in this study both for its global applications and its use by Canadian organizations such as the Canadian Institute for Health Information (CIHI), Health Canada, and the Patented Medicine Prices Review Board (PMPRB). The ATC system classifies drugs into groups at five levels. At level 1, medications are organized into anatomical main groups according to the organ or system on which they act. Levels 2, 3, and 4 indicate therapeutic, pharmacological, and chemical properties, respectively. Level 5 is specific to unique chemical substances.

Medications within a single CSG (level 4) are often used in the treatment of the same indication. Having therapeutic options allows the prescriber to determine the most appropriate therapy for an individual patient, in terms of tolerance, effectiveness, and other clinical considerations. For this reason, variation in provincial and territorial funding for medications at the CSG level is of even greater clinical relevance to prescribers and patients than differences in accessibility at the individual drug level. Variations in the numbers of CSGs listed in provincial and territorial for-

WHO ATC ANATOMICAL MAIN GROUPS	
A	Alimentary tract and metabolism
B	Blood and blood-forming organs
C	Cardiovascular system
D	Dermatologicals
G	Genitourinary system and sex hormones
H	Systemic hormonal preparations
J	Anti-infectives for systemic use
L	Antineoplastic and immunomodulating agents
M	Musculoskeletal system
N	Nervous system
P	Antiparasitic products, insecticides, and repellents
R	Respiratory system
S	Sensory organs
V	Various

KEY POINTS

- This study is the first to compare entire provincial formularies to assess accessibility across the provincial drug plans.
- It analyzes availability of public funding for groups of *chemically similar* medications (not individual products).
- It confirms previous analyses (using different methodology) that show *wide differences* across the provinces in access to publicly funded medications.
- Disparities include both the *comprehensiveness* of chemical subgroups as well as the therapeutic *distribution* of these subgroups as listed in the provincial formularies.
- British Columbians and Nova Scotians have access to the greatest number of chemical subgroups in provincial drug plans.
- This study is a potential resource for policy discussions regarding provincial (and/or potential national) formularies and potential national pharmacare.

— The Editors

ularies represent differences in the ability of patients to access not just individual medications, but entire groups of chemically similar drugs. This study analyzed the availability of public funding for groups of chemically similar medications, rather than separate drug products, to identify differences in drug accessibility for Canadian beneficiaries on the basis of their province of residence.

TABLE 1 — Sample coding for rofecoxib according to the World Health Organization Anatomical Therapeutic Chemical (WHO ATC) classification system

Level and description	No. of groups*	WHO ATC classification	Corresponding system or drug group
1st level: anatomical main group	14	M	Musculoskeletal system
2nd level: therapeutic main group	94	M 01	Anti-inflammatory and antirheumatic products
3rd level: pharmacological subgroup	265	M 01 A	Anti-inflammatory and antirheumatic products, nonsteroids
4th level: chemical subgroup	848	M 01 A H	Coxibs
5th level: chemical substance	3942	M 01 A H 02	Rofecoxib

*The number of distinct groups established by the WHO within the indicated level. For example, there are 14 anatomical main groups within the 1st level of the WHO classification system, and there are 3942 chemical substances at the 5th level.

Methods

The six Canadian provinces with the greatest public drug expenditures were selected for analysis: Alberta, British Columbia, Manitoba, Nova Scotia, Ontario, and Quebec.¹ The provincial formularies in effect as of April 1, 2003, were used (Table 2). ATC codes for medications listed in the provincial formularies were determined from the Drug Product Database (DPD) maintained by Health Canada⁶ and were verified with the chemical name and code listed by the WHO. Medications listed in provincial formularies that could not be located in the active section of the DPD were considered to be unavailable to Canadian residents and were excluded from the analysis. For all formulary products, we found the WHO ATC code assignments to be consistent with Health Canada's drug database.

Medications were identified as being full or restricted benefits. Full-listing medications were those to which beneficiaries had unrestricted opportunity for reimbursement. Restricted-listing medications were those for which administrative or clinical criteria had to be met before approval was granted for reimbursement.³ Formularies with subdivisions for distinct beneficiary populations were considered to have given a product listing status if at least one beneficiary group within the provincial drug program had access to the medication.

The British Columbia formulary includes a reference-based drug program. British Columbia patients eligible for PharmaCare benefits are entitled to full coverage for the preferred "reference" drug within a therapeutic category. Patients choosing a nonreference drug are responsible for the difference in price. Reference drugs, for which patients were eligible to claim full reimbursement, were considered as full-listing products (see box) as identified in the PharmaNet Drug Master complete drug list and the *Low Cost Alternative Reference Drug Program Booklet*. Restricted-listing products were identified in the British Columbia Limited Coverage Drug Program. Restricted-listing status also pertains to nonreference products for which patients may receive full reimbursement if special authority has been granted for exemption from the reference-based drug program.

For the purposes of this study, the status of a CSG was determined by the least restricted medication it contained. Hence, if a CSG included just one full-listing medication, it was categorized as a full-listing CSG. If none of the medications within a CSG were listed in a particular provincial formulary, then the CSG was categorized as "not listed." CSGs with a "not listed" status in all six provinces were removed from the analysis, which left 484 CSGs for the statistical comparisons.

The number of provincial formularies listing each CSG was tabulated to determine concordance in provincial listings, as follows:

- Core CSGs: having a full or restricted listing in all six provinces;

Formulary	Source	Formulary effective date
Alberta		
Alberta Health and Wellness Drug Benefit List	www.ab.bluecross.ca/dbl/publications.html#ahwdbl	Mar. 1, 2003
British Columbia		
PharmaCare <i>Low Cost Alternative Reference Drug Program Booklet</i>	www.hlth.gov.bc.ca/pharme/outgoing/booklet.pdf	Oct. 15, 2002
PharmaNet Drug Master complete drug list	www.hlth.gov.bc.ca/pharme/outgoing/pnp.pdf	July 7, 2003*
Limited Coverage Drug Program	www.healthservices.gov.bc.ca/pharme/sa/criteria/restricted/restrictedtable.html	July 7, 2003*
PharmaCare newsletters	www.healthservices.gov.bc.ca/pharme/newsletter/index.html	April 8, 2003 May 6, 2003 June 6, 2003
Manitoba		
Prescription Drug Costs Assistance Act, Parts 1 and 2	www.gov.mb.ca/health/mdbif/pdca39.pdf	May 1, 2003*
Bulletins	www.gov.mb.ca/health/mdbif/bulletins.html	May 1, 2003
Nova Scotia		
Nova Scotia Formulary	Nova Scotia Medical Services Insurance (902) 468-9700	April 1, 2003
Ontario		
Ontario Drug Benefit Formulary	www.health.gov.on.ca/english/providers/program/drugs/formulary/ed38_0_bk.pdf	Dec. 2, 2002
Quebec		
Liste de Médicaments Assurés	www.ramq.gouv.qc.ca/fr/professionnels/listmed/lm_tdmf.shtml	Mar. 14, 2003
*For British Columbia and Manitoba, the formulary was issued after study cutoff date of April 1, 2003. To ensure that the analysis correctly reflected information in effect at the cutoff date, formulary updates issued between April 1, 2003, and the publication date of the formulary were reversed on the basis of information published in provincial newsletters or bulletins (which are also listed in this table).		

- Shared CSGs: full or restricted listing in two to five of the selected provinces;
- Exclusive CSGs: full or restricted listing in only one of the selected provinces.

Interprovincial agreement of listing decisions was determined statistically on the basis of kappa coefficients, calculated in pairwise fashion to measure concordance between provincial coverage decisions. (According to Fleiss,⁷ kappa values greater than 0.75 represent excellent agreement beyond chance, values between 0.40 and 0.75 indicate fair to good agreement beyond chance, and values below 0.40 represent poor agreement beyond chance.)

Results

British Columbia and Nova Scotia provided residents with access to the greatest number of CSGs, while Manitoba listed the fewest. Figure 1 depicts the listing status of CSGs within the six provincial formularies in the analysis.

The therapeutic distribution of formulary drug benefits was determined by categorizing provincial CSG listing status within the 14 WHO ATC anatomical main groups (Table 3). The average number of CSGs in each provincial formulary, according to anatomical main groups, is depicted in Figure 2.

Commonality in provincial formulary listings was determined by quantifying the CSGs listed in all six provincial formularies. A total of 197 core CSGs were identified, representing 41% of all CSGs analyzed. In contrast, 84 (17%) of the CSGs had an exclusive listing, appearing in only one provincial formulary. Of these 84 CSGs, 27 were listed in the Nova Scotia formulary and 25 in the British Columbia drug formulary. Figure 3 depicts the numbers of core, shared, and exclusive CSGs on a provincial basis.

The level of interprovincial agreement in drug formulary listing status (i.e., pairwise kappa coefficients), ranged from 0.23 (between British Columbia and Quebec) to 0.45 (between Alberta and Manitoba) (Table 4). Kappa coefficients for nine of the 15 pairings fell below 0.40, indicating a poor level of agreement beyond chance. The other six kappa values represent only fair agreement beyond chance, being in the range of 0.40 to 0.45.

Discussion

This study reports large variation in drug accessibility for residents of six Canadian provinces. Disparities were observed in both the comprehensiveness of CSGs available in these provinces and the therapeutic distribution of CSGs listed in the provincial formularies. A poor level of interprovincial agreement in CSG listing status was indicated by kappa coefficients, a result consistent with previously published reports of interprovincial variation in Canadian drug formularies.^{3,4}

The findings of this study are unique in that they demonstrate interprovincial variation in formulary listings not just at an individual drug level, but also at the chemical subgroup level. This situation has clinical relevance to patients, in that whole drug categories are associated with differential access across provincial drug plans.

Variation in provincial drug formularies may be attributable to several factors that influence listing decisions. Economic considerations (e.g., cost-effectiveness analyses and budget impact analyses), comparative evaluations of effectiveness, demographics, government priorities, pharmaceutical policy strategies, and patient advocacy all play a role in formulary decisions.⁸⁻¹¹ Inconsistencies may also be due to flaws in the scientific evaluation process.¹² With each province making its own listing decisions, it is not surprising that differences exist at the chemical substance level.

The therapeutic implications of this study are even more significant, given the new evidence of substantial differences in provincial listings at the CSG level.

*Of all provinces,
British Columbia
and Nova Scotia
provide residents
with most CSGs*

FIGURE 1 — Provincial drug formulary listing status of chemical subgroups of the WHO ATC classification for selected Canadian provinces

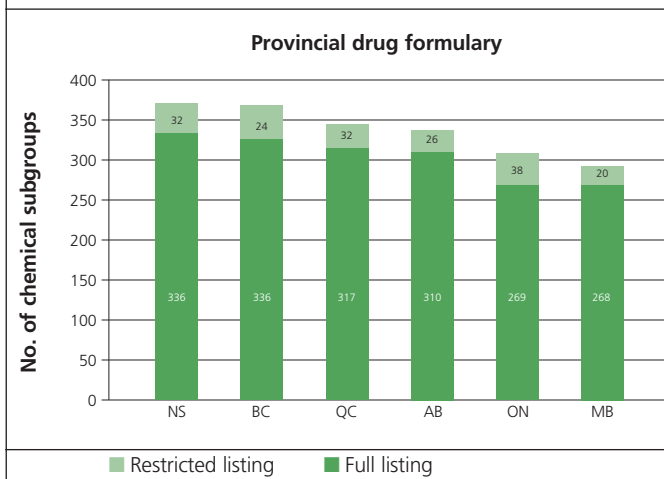


FIGURE 2 — Mean number of chemical subgroups of the WHO ATC classification in drug formularies of selected Canadian provinces, organized by anatomical main groups

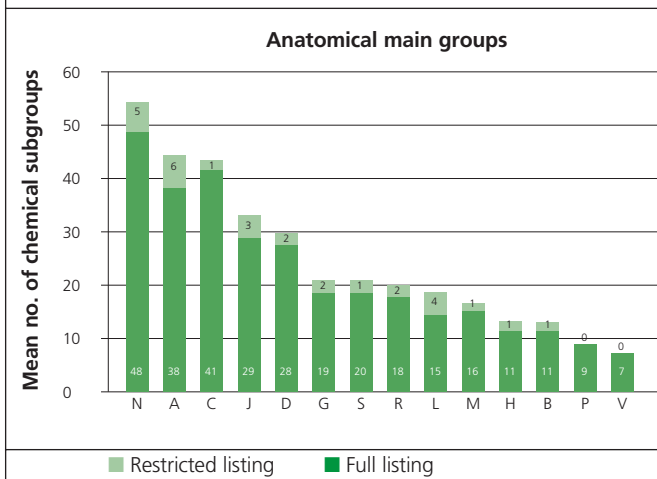


TABLE 3 — Therapeutic distribution of chemical subgroups of the WHO ATC classification with full-listing status*

		WHO ATC anatomical main group													
		A	B	C	D	G	H	J	L	M	N	P	R	S	V
No. of full-listing CSGs	TOTAL CSGS	72	20	53	45	30	14	45	29	23	67	16	28	24	15
	AB	43	9	40	31	23	11	24	3	18	54	8	19	22	5
	BC	52	13	46	28	20	12	34	8	17	53	9	18	19	7
	MB	29	9	39	22	15	8	24	23	12	43	8	15	17	4
	NS	40	12	43	31	19	12	32	20	20	45	8	20	22	12
	ON	30	8	39	23	18	10	25	19	13	40	7	15	19	3
	QC	35	13	36	30	18	11	33	16	16	51	13	19	18	8

*Data shown are the number of chemical subgroup groups with full-listing status for selected Canadian provinces, organized by anatomical main groups.
 †Total number of chemical subgroups (CSGs) within the designated anatomical main group for which at least one province had a full listing.

The interprovincial variation observed in this analysis may also result from differences in the beneficiary populations covered by provincial formularies. For example, Alberta provides the fewest full listings in anatomical main group L (the antineoplastic and immunomodulating agents), listing only three of the 29 CSGs. However, cancer medications not listed in the Alberta formulary may be accessible through the Alberta Cancer Board Outpatient Cancer Drug Benefit Program. A second analysis was conducted to address this issue (by excluding CSGs within anatomical main group L), but the overall kappa values did not change significantly. A complete investigation of the programs available for all special patient groups (e.g., those with HIV/AIDS, cancer, cystic fibrosis), in each province and territory would be desirable.

Provinces and territories also offer special authorization procedures through which qualified patients can access drugs not listed in the formulary. The current study excluded these procedures, because such decisions are made on an individual basis and are therefore not amenable to this type of comparative analysis.

Conducting this analysis at the fourth, rather than the fifth, level of the ATC classification did limit the degree of specificity. As such, provinces providing coverage for a single medication within a given CSG were not differentiated from provinces covering several medications in the same CSG. This study was designed to explore interprovincial variation with regard to groups of medications, and the study design was not meant to imply that all drugs within a CSG are equivalent. Individual response to medications in terms of effect and tolerance should not be understated, and patients stand to benefit the most when they have access to a variety of therapeutic choices within a CSG.

Restricted formulary listings have been used to help manage drug therapies that require special monitoring, are

associated with greater safety concerns, or are thought to require greater control because of their comparatively higher costs. In addition, the design of drug plans (in terms of deductibles, co-payments, maximum pricing schemes, and therapeutic interchange) can also result in restricted access. There is a need for further research to investigate the factors contributing to listing decisions and the impact of these and other pharmaceutical policies on medication use and patient health outcomes.

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FIGURE 3 — Exclusive, shared, and core status of chemical subgroups of the WHO ATC classification in drug formularies of selected Canadian provinces*

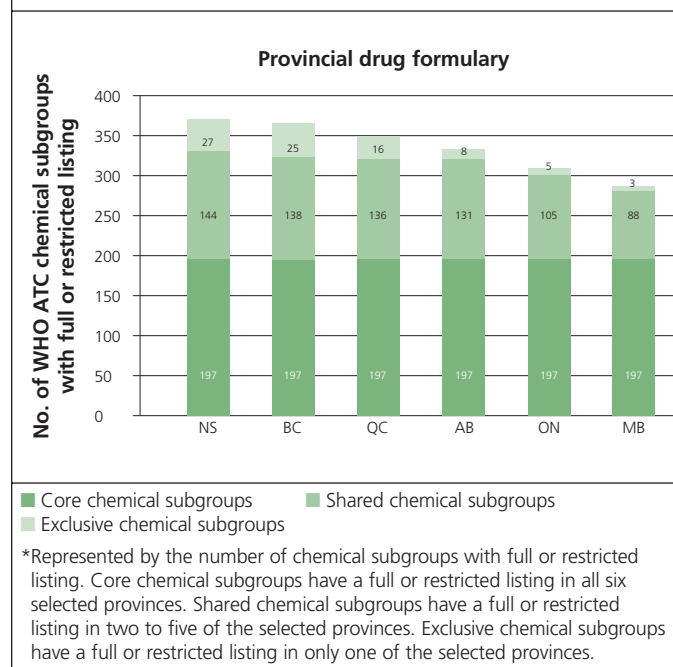


TABLE 4 — Kappa coefficients* for interprovincial agreement in the listing status of WHO ATC subgroups in the drug formularies of selected Canadian provinces

	AB	BC	MB	NS	ON	QC
AB		0.41	0.45	0.37	0.30	0.42
BC	0.41		0.33	0.29	0.34	0.23
MB	0.45	0.33		0.40	0.43	0.39
NS	0.37	0.29	0.40		0.32	0.33
ON	0.30	0.34	0.43	0.32		0.40
QC	0.42	0.23	0.39	0.33	0.40	

*Kappa coefficients were calculated using SPSS 12.0.1 for Windows. Values greater than 0.75 or so may be taken to represent excellent agreement beyond chance, values below 0.40 or so may be taken to represent poor agreement beyond chance, and values between 0.40 and 0.75 may be taken to represent fair to good agreement beyond chance.⁷

Conclusion

This investigation reports substantial interprovincial variation in drug formulary listings of CSGs for six selected Canadian provinces. Not only do patients across Canada lack access to the same medications within publicly funded drug programs, but there are also significant disparities in access to groups of chemically similar drugs. This finding emphasizes the need to provide comprehensive and equitable access to publicly funded pharmaceuticals. The results also provide a benchmark against which to measure the impact of a fully implemented Common Drug Review process. ■

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