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ACTIVITIES OF THE PAN-CANADIAN PHARMACEUTICAL ALLIANCE: AN OBSERVATIONAL ANALYSIS

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ABSTRACT

Background

The pan-Canadian Pharmaceutical Alliance (pCPA) was established in 2010 to negotiate confidential prices for drugs coming forward from Canada's centralized health technology assessment (HTA) agency reviews, on behalf of the participating public drug plans.

Objective

To analyze the activities of the pCPA, to determine: alignment of HTA agency recommendations and pCPA negotiation decisions; the role of health economics in pCPA activities; and patterns of implicit prioritization.

Methods

The analysis was based on the archive of drugs handled through the pCPA, as posted on its website. The period of observation was from inception to August 31, 2017. HTA recommendations were sourced from the websites of the Common Drug Review (CDR) and the pan-Canadian Oncology Drug Review. Descriptive and statistical analyses were conducted.

Results

The dataset contained 206 drug-indication pairings. There was close but imperfect alignment between HTA agency recommendations and the pCPA's decisions to negotiate; deviations occurred only with CDR-reviewed drugs. The median incremental cost-effectiveness ratio of negotiated drugs was $168K/QALY for oncology drugs, but $70K/QALY for non-oncology drugs. The time to initiate negotiations was dramatically shorter for oncology versus non-oncology drugs (mean 54 versus 263 days), and also differed between therapeutic

areas at CDR. The time required for PCPA activity was surprisingly similar for drugs recommended without a price condition and for those conditional on a price reduction.

Conclusion

These findings revealed a strong alignment between HTA recommendations and pCPA negotiations, an implicit prioritization favouring oncology drug negotiations, and an evolving role for health economics in Canada's reimbursement process.

Key Words: *drug reimbursement, price negotiation, economic evaluation, prioritization.*

The sustainability of drug funding is a perennial issue in the Canadian political landscape. Canada is widely misunderstood to have a universal public health care system, but it does not include outpatient drugs.[1] Outpatient prescription drug costs fall under a mosaic of payers, with only 42% paid for by public drug plans.[2] Health care funding (including public drug programs) is budgeted and administered predominantly at the provincial level. Each provincial drug plan varies in its comprehensiveness, with all including seniors (65+) and persons on social assistance, and some including the total population.

Sustainable, responsible public drug funding is enabled by a two-step national process. First, centralized health technology assessment (HTA) agencies review clinical and economic evidence submitted by manufacturers to make funding recommendations for all provinces (excluding Quebec). There are similar but separate HTA processes for oncology drugs (the pan-Canadian Oncology Drug Review [pCODR]) and for non-oncology drugs (the Common Drug Review [CDR]). Funding recommendations focus largely on clinical evidence; where the economic evidence is unsupportive, price reductions are requested to improve cost-effectiveness.[3,4] Increasingly a specific level of price discount is being suggested in CDR's recommendations.[5]

Subsequent to HTA review, another centralized process collectively negotiates listing agreements (generally involving confidential price discounts) with manufacturers: the pan-Canadian Pharmaceutical Alliance (pCPA). Each participating drug plan then implements funding decisions to align with the collective negotiated agreement.

The pCPA began informal operations in August 2010, established a formal office in September 2015, and is currently formalizing processes and guidelines. The founding principles of the pCPA were to: increase access to drug treatment options; achieve lower drug costs and consistent pricing; and improve consistency of coverage criteria across Canada.[6] Early research on the pCPA was preliminary and limited by the immaturity of available data.[7,8] It now appears that the pCPA has met several objectives. The pCPA reports that it collectively saves CDN$1.28B annually (although this finding has not been externally validated).[6] Shorter times to listing and more consistency of listing across provinces have been reported.[9,10]

While overall market access is improving, different rates of success for different drugs and/or therapeutic areas have been observed anecdotally. The pCPA has been under-resourced for most of its lifespan, with no formal office for its first five years and an organic process evolution As such, prioritization of activities has been a predictable if opaque occurrence. The factors driving any implicit prioritization have not been formally articulated or acknowledged.

The activities of the pCPA have not been analyzed from the perspective of their completed body of work. The timing of this research may help inform the pCPA itself as it develops formal guidelines from its current organic approach. Moreover, the national pricing regulatory agency in Canada (the Patented Medicines Pricing Review Board [PMPRB]) intends to add cost-effectiveness to guide pharmaceutical price regulation in 2019.[11] It may be instructive for the PMPRB to observe how the pCPA has used cost-effectiveness in its pursuit of value-based drug pricing.

The objective of this observational research was to analyze the activities of the pCPA, in order to determine: alignment of HTA agency recommendations and pCPA negotiation decisions; the role of health

economics in pCPA activities; and patterns of implicit prioritization at the pCPA.

METHODS

Activities of the pCPA were assessed based on the archive of its decisions posted on the organization's website.[6] The analysis first identified all drugs for which the pCPA had completed negotiation decisions. Of these, there were two categories: drugs for which negotiations were initiated (which could be either successfully completed or terminated without success) and drugs for which the decision was made not to negotiate. Drugs still in active negotiation (which lacked negotiation completion dates) and drugs which the pCPA decided to refer for individual provincial negotiation were excluded from the analysis. (This latter group generally were cases from earlier years when there had been substantial inter-provincial heterogeneity regarding pre-existing agreements for specific drug classes).

The period of observation was from inception of the pCPA to August 31, 2017. Archives were formally maintained starting in January 2014; for dates prior to this, the analysis was supplemented with a government-commissioned report that assessed early pCPA activities and included additional data points.[12] Manufacturers were contacted to obtain any remaining missing dates; 16 dates remained missing, with a 92% completion rate for paired negotiation dates (100% completion rate for all other variables). The archives and the report were not originally intended to report comprehensively all pCPA activities; however, examination of HTA recommendations showed that all HTA-reviewed drugs eventually entered the pCPA archives – if not for an initial indication, then for a subsequent indication.

Data inputs from the pCPA archives were: drug name, drug indication, negotiation decision (negotiated/did not negotiate [DNN]), date of decision whether or not to negotiate, and date of negotiation completion.[6] From these, two time periods were defined: the 'in consideration' phase (from posting of the final HTA recommendation to the pCPA decision whether to negotiate) and the 'negotiation' phase (from initiating to completing negotiations). The time spent 'in consideration' was exclusively at the discretion of the pCPA, while 'negotiation' time was confounded by multiple external factors, such as the pace of the manufacturer. It was hypothesized that the duration of time 'in consideration' was a proxy for implicit prioritization – that is, the provinces would move more quickly to open negotiations for drugs perceived to have higher priority.

Health Canada's website was used to determine the date of regulatory approval (the Notice of Compliance [NOC]).[13] HTA recommendations were examined to provide the remaining data inputs. Recommendations and their reasons were sourced from the websites of the two relevant agencies (CDR and pCODR).[14] Data abstracted from these websites included: HTA recommendation (list/do not list [DNL], date of recommendation, presence of price conditions, submission variables (HTA agency, type of submission, priority review status, submission prior to regulatory approval), drug variables (name, indication, therapeutic area, manufacturer), and economic variables (incremental cost-effectiveness ratio [ICER] as reported by the manufacturer and/or recalculated by the HTA agency, statement regarding the extent of price reduction required). HTA agencies uniformly reported all aforementioned variables, with the excep-tion of the economic variables. Reporting of ICERs was inconsistent, and conduct of a threshold analysis was at the discretion of the economic reviewer.

The list of data variables and their definitions are provided in Appendix Table 1. However, two key variables are described herein. First, HTA recommendations can be either 'DNL' or 'list', often with various conditions, most commonly clinical criteria and/or price (for example, list conditional on a price reduction to achieve acceptable cost-effectiveness). All types of positive list recommendations were combined to dichotomize versus DNL. Second, manufacturers provide economic analyses for all submissions, many of which are cost-utility analyses that generate an ICER. The HTA agency's economic reviewers often re-calculate the ICER based on an alternate set of assumptions. Both the manufacturer's submitted ICER and the HTA agency's recalculated ICER were considered where available.

Data abstraction for ICERs from the HTA websites was complicated: ICERs could be redacted, or not

reported, or difficult to interpret if there were multiple comparators. Where a range was reported instead of a point estimate, the lower value was included in the analysis (applied to both ICERs [since upper values were typically speculative tests] and suggested price discounts [to be conservative]). Where the ICER result was dominance or dominated, this had no numerical translation and was excluded. The economic reviewer's reports were sourced where available to supplement the data in the recommendation. pCODR's economic reviews were routinely posted in a timely manner, and became uniformly structured over time, which yielded more data points for abstraction than CDR economic reviews (which lacked these features).

Database clean-up involved several steps. HTA agencies review each drug indication as a separate submission and make unique recommendations for each indication. However, the pCPA may have negotiated multiple indications for one drug at the same time (n=9). In such cases, each individual indication was considered separately, adding to the total count of negotiations. Drug indications which had no HTA recommendation were removed (n=6). Negotiations related to agalsidase alfa and beta were excluded as these were highly atypical re-negotiations, occurring a decade after their HTA recommendations (n=4).

The pCPA considered some drug indications on multiple occasions, for a variety of reasons. Commonly, a resubmission changed the original HTA recommendation and triggered new negotiations. In a few instances, the CDR conducted a broad therapeutic review in a disease area (such as hepatitis C), which prompted therapeutic class re-negotiations. In several other cases, repeat negotiations would be conducted after expiry of the term-limited initial contracts. Increased competition in a therapeutic category could also inspire class-level re-negotiations. In all these cases, only the most recent HTA submission associated with the current negotiation status was considered. The final database comprised 206 unique drug indications.

Descriptive analyses were conducted. ICERs were a unique variable in that they were highly skewed with a few extreme high values affecting mean results. As needed, a median and a trimmed mean were used to exclude outliers (ICERs ≥ $1M/QALY).

Statistical analyses were conducted on all numerical comparisons. Pair-wise comparisons were conducted using Student's t-tests for mean values and Mann-Whitney U tests for comparisons of median values. The Chi-Square Test of Independence was used for nominal variables, and the Fisher Exact test was used instead when the number of observations in one category was too small. Multiple groups were assessed using the Pearson's correlation test. All analyses were conducted using SAS and XLSTAT software (Addinsoft, New York). Differences were considered statistically significant if $p < 0.05$. Given the exploratory nature of the analysis, no adjustment for multiplicity was included.

RESULTS

Of the 206 drug indications examined in the database, 53 (26%) were not negotiated (DNN) and 153 (74%) were selected for negotiation – of which 141 (92%) were completed successfully. The rate of successful negotiation was 89% (91/102) for CDR-reviewed drugs and 98% (50/51) for pCODR-reviewed drugs. Most unsuccessful negotiations occurred in the last two years.

The relationship between the HTA recommendation and the decision to negotiate differed by agency. The decision whether or not to negotiate corresponded precisely with list/DNL recommendations for pCODR (100% alignment) but less precisely for CDR (86% alignment overall – Table 1). Exceptions were found in each year of operation, with 5 of the 19 discrepancies occurring in 2017, suggesting some continuing deviation from the pCPA's nominal processes.

Fully 25% of DNL recommendations from the CDR were ultimately negotiated – an unexpected finding, given the pCPA's fundamental 'no means no' tenet.[15] All 10 instances of a decision not to negotiate a list recommendation occurred when a price-reduction condition was present.

While both agencies frequently impose a condition of a price reduction, there were 17 instances when an HTA agency (exclusively the CDR) explicitly stated the extent of price reduction recommended (a threshold analysis). There were 12 list recommendations with a threshold analysis; for the eight that were negotiated, the mean suggested reduction was 35% (versus 57% for

those that were not negotiated (p=0.36). The remaining five threshold analyses were DNL recommendations that were uniformly rejected for negotiation (mean suggested reduction: 74%).

Both manufacturer-submitted and HTA-recalculated ICERs were abstracted (Table 2). Although economic evaluations are required for all submissions, not all submissions required a full cost-utility analysis, nor were ICER results consistently reported in posted recommendations, whether or not they were submitted or re-analyzed.

The HTA-recalculated ICERs were higher than those submitted by the manufacturer (p=0.01), but the extent of discrepancy varied. The ratio of recalculated ICERs to submitted ICERs was higher at CDR than at pCODR (p=0.02). Subsequent analyses examined only HTA-recalculated ICERs, assuming that these (rather than manufacturer-submitted ICERs) informed pCPA activities.

Mean ICERs were skewed by five values at or above $1M/QALY. (All were CDR drugs, and two were negotiated – only one successfully). Median ICERs are reported in Figure 1 and were consistent with a trimmed mean which excluded these extreme values.

The data in Figure 1 illustrate three distinct findings. For pCODR drugs, the decision to negotiate (and by extension, the HTA recommendation) was not affected by the ICER estimate (p=0.41). On the other

TABLE 1 Alignment between Negotiation Decisions and HTA Recommendations

HTA Agency	List		Do Not List		Total (n=206)
	Negotiate	DNN	Negotiate	DNN	
pCODR	51 (76%)		16 (24%)		67 (33%)
	51 (100%)	0 (0%)	0 (0%)	16 (100%)	
CDR	103 (74%)		36 (26%)		139 (67%)
	93 (90%)	10 (10%)	9 (25%)	27 (75%)	

CDR = Common Drug Review; DNN = do not negotiate; HTA = health technology assessment; pCODR = pan-Canadian Oncology Drug Review.

TABLE 2 Comparison between Manufacturer-Submitted and HTA-Recalculated Mean ICERs

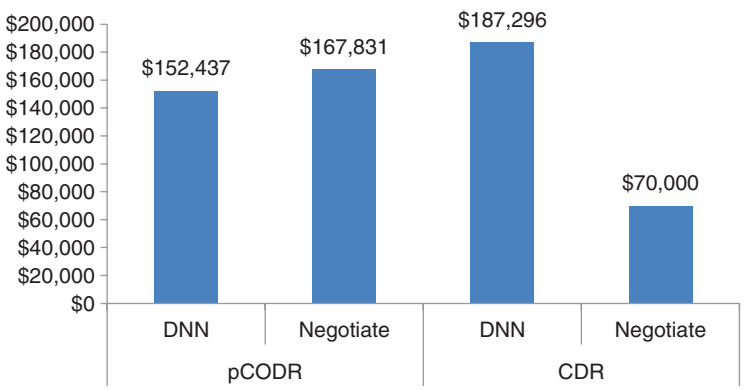
HTA Agency	Recommendation	Mean ICER				Ratio, HTA:Manu.
		n	Manufacturer	n	HTA	
CDR	Do Not List	18	$175,395	13	$760,650	3.4
	List	36	$223,571	34	$336,310	2.9
	Do Not Negotiate	18	$329,477	16	$753,226	3.5
	Negotiate	36	$146,530	31	$299,077	2.9
pCODR	Do Not List/Negotiate	15	$104,826	14	$156,205	1.7
	List/Negotiate	47	$129,832	46	$179,481	1.8

CDR = Common Drug Review; HTA = health technology assessment; ICER = incremental cost-effectiveness ratio; Manu. = manufacturer; pCODR = pan-Canadian Oncology Drug Review.

hand, the negotiation decision was highly affected by the ICER for CDR drugs (p=0.05). Furthermore, oncology drugs were negotiated despite ICERs that were considered unattractive for non-oncology drugs. There was no significant difference between the median ICERs of pCODR drugs accepted for negotiation and CDR drugs rejected for negotiation (p=0.62). The willingness to negotiate drugs at ICERs well above any conventional level of acceptability might indicate the scale of discount sought by the pCPA.

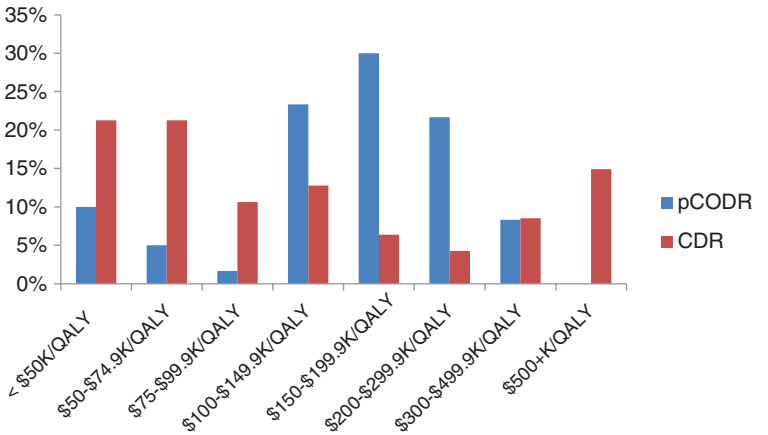
The willingness to negotiate oncology drugs at higher ICERs can be partly understood by examining the ICER distribution (Figure 2). These differed substantially between agencies. Oncology drug ICERs mostly fell between $100-$300K/QALY (75% of reported values, Figure 2). CDR-recalculated ICERs were bimodal: only 23% fell in the $100-$300K/QALY range, with 53% under $100K/QALY and 15% over $500K/QALY.

FIG. 1 Median HTA-Recalculated ICERs by negotiation status and HTA agency.



X axis: HTA Agency/Negotiation Decision
Y axis: Cost/QALY (quality-adjusted life year)
CDR = Common Drug Review; pCODR = pan-Canadian Oncology Drug Review.

FIG. 2 Distribution of HTA-Recalculated ICERs by HTA Agency.



X axis: ICER range (incremental cost effectiveness ratio)
Y axis: Per Cent
CDR = Common Drug Review; pCODR = pan-Canadian Oncology Drug Review; QALY = quality-adjusted life year.

Within each HTA agency, ICERs also differed by therapeutic area, especially for CDR. Table 3 displays the rate of negotiation and the mean HTA ICER by therapeutic area for CDR. At pCODR, ICERs were not discriminatory between negotiation decisions, were all within a similar range of values and were not informative.

As per Figure 3, the number of days required for the 'in consideration' phase differed substantially by HTA agency (P=0.02) though the difference for negotiation time did not (P=0.18). Total time required for both phases of negotiation was half the time for oncology versus non-oncology drugs, owing almost entirely to the different durations of the 'in consideration' phase (P=0.01) – a phase entirely at the discretion of the pCPA – and presumed to indicate implicit prioritization.

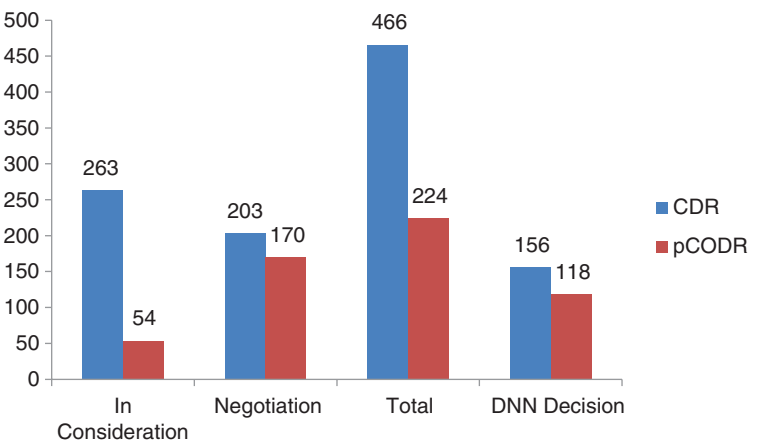
The decision not to enter a negotiation was also faster with pCODR drugs (118 days versus 156 days

TABLE 3 Negotiation Rate and Mean ICER by Therapeutic Area – CDR

Therapeutic Area	Negotiation Rate	Mean HTA ICER - Negotiated	Mean HTA ICER – Not Negotiated
Antiviral	100%	$41,660	Not applicable
Autoimmune	68%	$89,667	$515,795
Cardiovascular	71%	$66,384	None available
CNS	71%	$55,979	$226,410
Endocrinology	73%	$65,313	None available
Other	58%	$74,130	$135,558
Rare	57%	$1,671,123	$2,706,872
Respiratory	100%	$279,986	Not applicable

CNS = central nervous system; HTA = health technology assessment; ICER = incremental cost-effectiveness ratio.

FIG. 3 Days Required for pCPA Activities by HTA Agency



X axis: Negotiation Phase
Y axis: Number of Days
CDR = Common Drug Review; DNN = do not negotiate; pCODR = pan-Canadian Oncology Drug Review.

for CDR drugs, not significant [P=0.32]). Given the perfect concordance with pCODR recommendations, 118 days seemed long for a negotiation decision that may have been essentially routine.

Curiously, the number of days required for pCPA activities was virtually identical whether or not the recommendation included a price reduction condition: 424 days regardless of condition with CDR drugs, and 224 (with) versus 227 (without) for pCODR drugs (not significant, P=0.98). For CDR drugs only, the 'in consideration' period was 50 days slower for drugs recommended without a price condition, and 50 days faster in the negotiation phase.

As with ICERs, there was considerable variation in the number of days for pCPA activities by therapeutic area. Figure 4 shows the days at CDR, with the 'in consideration' phase varying from 38 days (antiviral drugs – largely the new hepatitis C direct-acting antivirals) to 647 days (endocrinology – largely oral antidiabetics), (P<0.001). Conversely, variation at pCODR (not presented) was minimal, ranging from 34 days for lung cancer to 75 days for other cancers (not significant, P=0.56). All pCODR therapeutic areas spent less time 'in consideration' than all CDR therapeutic areas except antiviral and respiratory drugs.

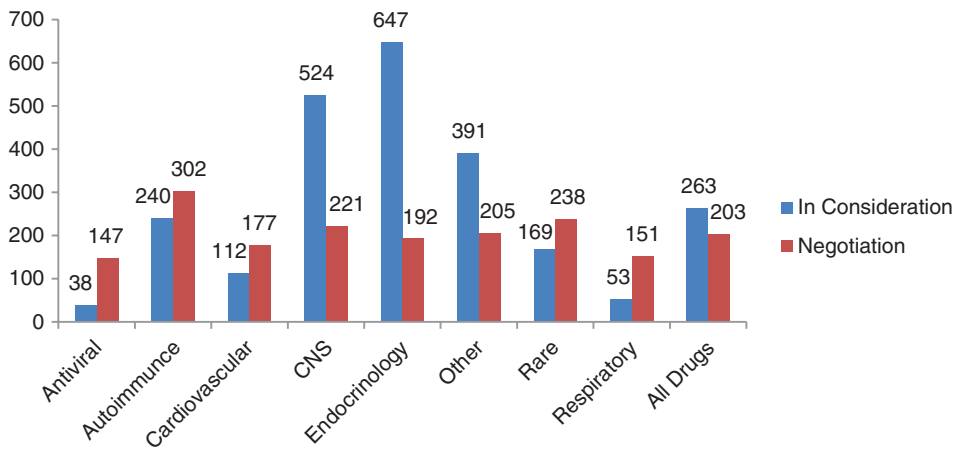
A lack of correlation between ICERs and days 'in consideration' was identified for both agencies; value for money (cost-effectiveness) was not associated with prioritization (Pearson correlation score of 0.01, p=0.98).

DISCUSSION

This research revealed interesting findings for each of its three objectives. First, it showed that pCPA negotiation activities closely followed HTA recommendations, with some divergence seen with CDR drugs. Second, faster negotiations were strongly associated with oncology drugs, while slower-than-expected negotiations were conducted for drugs recommended without a price condition and within select therapeutic areas. Finally, pCODR recommendations and pCPA negotiations for oncology drugs did not discriminate based on ICERs, while ICERs were discriminatory for non-oncology drugs. ICERs did not affect the time to initiate negotiation for either agency. These findings require deeper understanding and interpretation within the context of the Canadian landscape.

The perfect alignment between pCODR recommendations and negotiation decisions is noteworthy, and may be a product of at least two factors. First, the provincial drug plans and cancer agency managers contribute to both the pCODR review and the

FIG. 4 Days Required for pCPA Activities by Therapeutic Area – CDR



X axis: Therapeutic Area
Y axis: Number of Days
CNS = central nervous system.

subsequent negotiation, which may provide greater understanding of the dossier before negotiation decisions. There is no obvious systemic reason why CDR could not benefit from greater involvement of the drug plans in the HTA process. Second, the singular focus on cancer facilitates greater disease-relevant expertise among both the pCODR expert review board and the cancer agencies' executive.

CDR recommendations were subject to inconsistent negotiation decisions in both directions. Such inconsistency can give rise to increased uncertainty for stakeholders. The decision to negotiate a DNL may have reflected a willingness of the drug plans to consider non-evidentiary factors such as unmet need and rule of rescue. Conversely, in the case of positive recommendations that did not lead to negotiations, a high suggested price reduction may have left both parties with little enthusiasm to seek a negotiation.

Recommendations conditional on price reduction were a feature of both HTA agencies – since inception for pCODR, and since late 2012 for CDR. Further, CDR began making specific price reduction recommendations based on threshold analyses conducted by the economic review team. HTA reanalysis of the submitted economic model adopt conservative assumptions, generating significantly more pessimistic results. Since the pCPA does not conduct their own reanalyzes, the price reduction recommendation has become an important feature of the negotiations, representing an anchor value from the perspective of the payers. Consequently, the anonymous economic reviewers wield significant power within the continuum of the drug reimbursement process – despite a lack of accountability and inevitable use of subjective judgment.[16]

In this analysis, ICERs did not significantly affect the negotiation decision for pCODR-reviewed drugs, while there was strong evidence of a link for CDR-reviewed drugs. This finding was not surprising, given the overriding emphasis pCODR has always placed on clinical benefit in their deliberative framework. If clinical benefit was deemed to be present, then there appeared to be a willingness to move to negotiations, irrespective of the ICER.

ICERs that would have generated at least a strong signal against funding (with a high suggested discount), if not a negative recommendation at CDR, did not negatively influence pCODR reviews. DNL recommendations were based on clinical reasons alone at pCODR; they were based on either or both clinical and economic concerns at CDR.

This analysis defined the "in consideration" phase as a proxy for the prioritization accorded submissions by the provincial plan managers, assuming that a longer delay in uptake was due to the lower priority attached to the file. The pCPA maintains that a longer delay may reflect the complexity of a submission, particularly for highly disruptive or innovative technologies, and the need for preparation on the part of the public plans – potentially leading to shorter negotiation time overall.[17] The findings of this analysis did not support this explanation in the aggregate.

There are additional explanations for delay in specific cases. The launch of more than one drug for the same indication may cause the first submission to be delayed to facilitate class negotiations, or to apply strategic pressure on all sellers within a class. As well, a drug may have multiple new indications over a short time frame, in which case the drug negotiation might be delayed until after the HTA review of the final new indication.

Nevertheless, it was apparent from the data that cancer drugs waited a shorter time "in consideration". At CDR, therapeutic area was a weak proxy for unmet need; endocrinology, for example, could suggest a perceived lack of unmet need in diabetes, while antivirals were represented by the game-changing, curative and rapidly-funded Hepatitis C therapies. Some CDR-reviewed therapeutic areas were essentially treated as commodity markets, where inter-product innovation was perceived as modest. Finally, the number of days 'in consideration' was not shortened without a price reduction condition – a paradoxical finding. This could be explained by the fact that HTA agencies viewed only list prices – which might appear competitive - while pCPA was aware of negotiated prices.

This analysis relied on publicly available information for the majority of its data, supplemented by information provided by manufacturers. As such, there were several limitations. The PCPA archive was not established or intended for scientific research purposes. A careful review of all drugs that passed

through an HTA agency during the period of PCPA activity showed that every drug eventually came to the attention of the pCPA. However, there may have been multiple HTA reviews for any given drug; only the HTA recommendation associated temporally with the most recent pCPA negotiation was included. Dates in the pCPA archives were imprecise, and generally later than the dates of actual activities. The HTA archives had some data limitations as well.

The pCPA has clearly been successful in achieving its primary objective: to facilitate consistent access at lower prices for new entrants to the Canadian public drug plan market. This analysis could not assess whether the needs of patients and other important stakeholders were being appropriately met: if unmet health needs were prioritized, if health care budgets became more sustainable, and whether pharma companies achieved adequate commercial opportunities to encourage new drug launches in Canada.

In the near future, many important shifts may occur in the Canadian drug pricing and reimbursement landscape. PMPRB reforms may include cost-effectiveness to determine value for high-priority drugs, potentially changing the list price for these drugs outside of confidential negotiations exclusive to the public market.[11] National pharmacare has more traction than ever, with Parliament's Standing Committee on Health recently recommending its establishment.[18] The roles and processes of the agencies analyzed in this report – primarily the pCPA, and secondarily the HTA agencies – may continue to evolve in substantive ways going forward. Further research could focus on the impact of change compared to the benchmarks established in the current research.

CONCLUSION

This analysis documented the activities of the pCPA based on the final negotiation status of over 200 drug-indications considered since its establishment in 2010. The analysis revealed strong alignment with HTA recommendations, although deviations were seen for CDR-reviewed drugs. Oncology drugs benefited from faster access despite relatively unattractive ICERs. Non-oncology drugs displayed a clearer gradient for ICER acceptability, with a presumptive threshold below $100,000/QALY, and for greater discrepancy between submitted versus HTA reviewer-recalculated ICERs, both of which seemed to impact negotiations. Prioritization was also evident among non-oncology therapeutic classes, presumably based on perceived unmet need. Future research may document different patterns, as the pCPA and the Canadian reimbursement landscape continue to evolve.

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APPENDIX

Appendix Table 1. Database Variables

Variable	Source	Definition
Date of market approval	Health Canada	Date of issuance of a Notice of Compliance (+/- Conditions).
Start of negotiations[1]	PCPA Archives	Date of placement on either (1) 'active negotiations' list or (2) 'not to negotiate' list.
End of negotiations[1]	PCPA Archives	Date of placement on 'completed and closed negotiations' list.
Drug indication	PCPA Archives HTA Agency	As stated.
HTA recommendation	HTA Agency	Do not list = do not list. List = List, list in a similar manner, list with conditions or criteria, do not list at the submitted price.
Date of recommendation	HTA Agency	Date of final recommendation.
Conditions	HTA Agency	Either clinical or price or both.
HTA Agency	HTA Agency	pCODR (oncology) or CDR (non-oncology).
Type of submission	HTA Agency	Initial or Resubmission.
Priority review	HTA Agency	Granted priority review, requested but not granted, not requested.
Pre-NOC status	HTA Agency	HTA submission prior to NOC as stated by HTA agency and confirmed by Health Canada NOC date.
Therapeutic area	HTA Agency	As stated by pCODR or as categorized by analysts for CDR.
Manufacturer	HTA Agency	As stated; frequent manufacturer = 5 or more drug indication negotiation decisions at pCPA.
ICER – manufacturer[2]	HTA Agency	As reported by the HTA Agency's economic reviewer.
ICER – HTA Agency[2]	HTA Agency	As recalculated by the HTA Agency's economic reviewer.
Threshold[2]	HTA Agency	As reported by the HTA Agency's economic reviewer; the price discount required for cost-effectiveness.
Days 'in consideration'	Calculated	Days from HTA recommendation to start of negotiations.
Days 'negotiation'	Calculated	Days from start to end of negotiations.

[1] *PCPA archives are updated once monthly, at month-end, therefore PCPA dates are approximate.*
[2] *Where a range was provided instead of a point estimate, the lower limit of the range was used.*
HTA = health technology assessment; PCPA = pan-Canadian Pharmaceutical Alliance.