Strategies to reduce out-of-pocket medication costs for Canadians with peripheral arterial disease

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Background: Given that peripheral arterial disease (PAD) disproportionately affects people of lower socioeconomic status, out-of-pocket expenses for preventive medications are a major barrier to their use. We carried out a cost comparison of drug therapies for PAD to identify prescribing strategies that minimize out-of-pocket expenses for these medications.

Methods: Between March and June 2019, we contacted outpatient pharmacies in Hamilton, Ontario, Canada, to assess pricing of pharmacologic therapies at dosages included in the 2016 American College of Cardiology/American Heart Association guideline for management of lower extremity PAD. We also gathered pricing information for supplementary charges, including delivery, pill splitting and blister packaging. We calculated prescription prices with and without dispensing fees for 30-day brand-name and generic prescriptions, and 90-day generic prescriptions.

Results: Twenty-four pharmacies, including hospital-based, independent and chain, were included in our sample. In the most extreme scenario, total 90-day medication costs could differ by up to $1377.26. Costs were affected by choice of agent within a drug class, generic versus brand-name drug, quantity dispensed, dispensing fee and delivery cost, if any.

Conclusion: By opting for prescriptions for 90 days or as long as possible, selecting the lowest-cost generic drugs available in each drug class, and identifying dispensing locations with lower fees, prescribers can minimize out-of-pocket patient medication expenses. This may help improve adherence to guideline-recommended therapies for the secondary prevention of vascular events in patients with PAD.

Contexte : La maladie artérielle périphérique (MAP) affectant de manière disproportionnée les personnes à faible statut socioéconomique, les dépenses personnelles liées aux médicaments préventifs restreignent fortement leur utilisation. Nous avons comparé les coûts des traitements médicamenteux de la MAP pour cerner des stratégies de prescription qui réduisent au minimum les dépenses personnelles associées.

Méthodes : Entre mars et juin 2019, nous avons contacté des pharmacies pour patients externes à Hamilton (Ontario, Canada) afin d'évaluer la tarification de traitements pharmacologiques aux doses incluses dans la ligne directrice de prise en charge de la MAP des membres inférieurs publiée en 2016 par l'American College of Cardiology et l'American Heart Association. Nous avons aussi recueilli des informations sur les frais supplémentaires, dont ceux pour la livraison, la coupe des comprimés et l'emballage. Nous avons calculé le prix d'un approvisionnement de 30 jours de médicaments d'ordonnance génériques et de marque et d'un approvisionnement de 90 jours de médicaments d'ordonnance génériques avec et sans frais d'exécution d'ordonnance.

Résultats : Notre échantillon comprenait 24 pharmacies, dont des pharmacies d'hôpital, indépendantes et faisant partie d'une chaîne. La différence la plus élevée pour le prix total d'un approvisionnement de 90 jours de médicaments a atteint 1377,26 $. Les paramètres de variation des coûts comprenaient l'agent choisi dans une classe de médicaments, l'emploi d'un médicament générique ou de marque, la quantité délivrée, les frais d'exécution d'ordonnance et les frais de livraison, le cas échéant.

Conclusion : Pour réduire au minimum les dépenses personnelles liées aux médicaments, les médecins prescripteurs peuvent privilégier une ordonnance de 90 jours ou d'une durée aussi longue que possible, choisir les médicaments génériques les moins chers dans chaque classe et repérer les établissements de distribution aux frais inférieurs. Cela peut améliorer l'adhésion aux thérapies recommandées par la ligne directrice pour la prévention secondaire d'accidents vasculaires chez les patients atteints de MAP.

An estimated 1.5 million Canadians older than 40 years live with symptomatic peripheral artery disease (PAD), and globally it affects more than 230 million people, a burden that will rise substantially with the increasing prevalence of diabetes and smoking in developing countries.[1] Peripheral artery disease has a similar prevalence as and worse prognosis than coronary artery disease but is the least-screened and least-treated manifestation of atherosclerosis.[1–3]

Although considerable resources are allocated to develop novel therapeutic approaches for atherosclerosis, the underuse of established guideline-recommended secondary prevention therapies remains a driving factor for excess adverse cardiovascular events in PAD.[4] There has been insufficient focus on ensuring this optimal medical treatment. Studies have consistently documented substantial underuse of proven antithrombotic therapies and other secondary prevention medications (statins and angiotensin-converting-enzyme inhibitors), as well as poor uptake of smoking cessation strategies.[5,6] Paradoxically, although patients with PAD experience nearly double the rate of major adverse cardiac events as patients with coronary artery disease, they are prescribed preventive medications at almost half the coronary artery disease rate.[7] This disparity is associated with substantial additional cost. A Canadian study showed that the mean cost of a hospital stay for patients with any coronary artery disease was $1743, compared to $4677 for patients with PAD.[8]

Importantly, it has been reported that improved implementation of secondary prevention therapies in patients with PAD is associated with reduced all-cause mortality.[9] Consequently, improving uptake of existing therapies could lead to substantial benefit.

Given that PAD disproportionately affects people of lower socioeconomic status, out-of-pocket expenses for medications are a major barrier to their use.[10] Practical strategies to reduce medication costs are urgently needed to improve uptake of risk-reduction therapies.

We carried out a cost comparison of drug therapies for PAD to identify prescribing strategies that minimize out-of-pocket expense for these life-saving medications.

Methods

The Hamilton Integrated Research Ethics Board waived the need for formal ethics approval for this study.

Between March and June 2019, we contacted outpatient pharmacies in Hamilton, Ontario, Canada[11] to assess pricing of pharmacologic therapies for PAD at evidence-based dosages included in the 2016 American College of Cardiology/American Heart Association guideline for management of lower extremity PAD.[12] We also gathered pricing information for supplementary charges, including delivery, pill splitting and blister packaging. Pharmacies responded to a standardized questionnaire (Appendix 1, available at www.canjsurg.ca/lookup/doi/10.1503/cjs.003722/tab-related-content). We calculated prescription prices with and without dispensing fees for 30-day brand-name and generic prescriptions and 90-day generic prescriptions. When multiple generic or brand-name options of the same drug were available, we selected the cheapest option. We estimated the average annual household income of the postal code in which the pharmacies were located based on Canadian Census data.[13] To assess generalizability, we sampled pharmacies in Toronto, Ontario, and Winnipeg, Manitoba, using identical methods. All prices are presented in Canadian dollars. The perspective of an independent patient paying out of pocket was taken in all cases.

Results

We contacted 24 pharmacies: 4 hospital-based, 16 chain-based and 4 independent (Table 1). The average annual household income of the postal code in which the pharmacies were located ranged from $41 396 to $190 813.

We observed substantial variation in cost for each individual agent, as well as variation between drugs in the same class (Table 2) and between brand-name drugs and the generic version (Table 3).[14] Differences in cost for 90-day supplies of the same single agent sold at different pharmacies and/or produced by 2 different companies ranged from $11.55 to $57.23 for generic drugs and from $45.51 to $650.07 for brand-name drugs. Results for pharmacies in Toronto and Winnipeg did not appear to differ substantially from those for Hamilton (data not shown).

Dispensing fees ranged from $3.89 to $13.00 (Table 1) and were charged per medication fill/refill; this resulted in tripled fees for 30-day versus 90-day prescriptions. Delivery service was offered by 20 pharmacies (83%), at no added cost in 16 of the 20 (80%). Pill splitting and blister packaging were offered by 23 pharmacies (96%), at no additional cost in all cases.

Net cost difference

The maximum potential 90-day cost difference for guideline-based[12] medical PAD therapy consisting of an angiotensin-converting-enzyme inhibitor/angiotensin receptor blocker, a statin, and either clopidogrel monotherapy or low-dose rivaroxaban and acetylsalicylic acid (ASA) was $1377.26 (Table 4). When we included only generic medication options, the maximum potential 90-day cost difference was $106.18 (Table 5).

Discussion

We found substantial variation in the cost of medications within the same drug class for secondary prevention in

Table 1. Description of participating pharmacies

Identification	Type	Local average household income, $*	Dispensing fee, $	Delivery	Independent pricing†
A	Hospital-based	98 759	11.99	Fee associated	Yes
B	Hospital-based	47 483	11.99	No cost	No
C	Hospital-based	67 295	11.99	Fee associated	Yes
D	Hospital-based	86 440	11.99	Fee associated	No
E	Chain (Shoppers Drug Mart)	96 572	11.99	No cost	Yes
F	Chain (Shoppers Drug Mart)	47 483	11.99	No cost	Yes
G	Chain (Rexall)	104 640	12.99	No cost	Yes
H	Chain (Rexall)	46 369	9.99	No cost	Yes
I	Chain (Walmart)	76 431	9.97	No delivery	No
J	Chain (Walmart)	57 528	9.97	No delivery	No
K	Chain (Costco)	137 452	3.89	No delivery	No
L	Chain (Costco)	89 360	3.89	No delivery	No
M	Chain (Loblaw)	74 464	10.49	No cost	No
N	Chain (Loblaw)	114 061	10.49	No cost	No
O	Chain (Guardian/IDA)	41 396	10.99	Fee associated	Yes
P	Chain (Guardian/IDA)	190 813	11.99	No cost	No
Q	Chain (Pharmasave)	52 509	11.99	No cost	Yes
R	Chain (Pharmasave)	120 857	5.00	No cost	No
S	Independent	63 616	8.99	No cost	Yes
T	Independent	87 026	10.99	No cost	Yes
U	Independent	104 640	11.99	No cost	No
V	Independent	120 857	12.99	No cost	Yes
W	Chain (Costco)	84 784	4.49	No cost	No
X	Chain (Shoppers Drug Mart)	55 625	13.00	Free	No

*Before tax. Source: 2016 Canadian Census.[13]
†Prices are set by local dispensing locations rather than a centralized office.

Table 2. Cost range for 90 days for all peripheral artery disease medical therapy options in each guideline-recommended[12] drug class*

Drug class	Cost, $		Cost difference, $
	Lowest-cost agent*	Highest-cost agent*	
Angiotensin-converting-enzyme inhibitors	7.94 (generic ramipril)	747.00 (brand-name lisinopril)	739.06
Angiotensin receptor blockers	15.54 (generic valsartan)	452.70 (brand-name valsartan)	437.16
Antiplatelet agents	10.35 (generic ASA)	384.03 (brand-name clopidogrel)	373.68
Direct factor Xa inhibitors	129.15 (brand-name rivaroxaban)	Only 1 agent available	—
Statins	19.71 (generic rosuvastatin)	384.30 (brand-name atorvastatin)	364.59

ASA = acetylsalicylic acid.
*Cost represents that of the maximum evidence-based dosage of each drug and does not include dispensing or shipping fees.

patients with PAD. Cost differences were driven by choice of agent, generic versus brand-name drug selection, quantity dispensed and where medications were ultimately dispensed from. By selecting the least expensive options, prescribers could reduce the cost of secondary prevention medication by up to $1377.26 every 90 days. When we considered only generic medication options, the patient cost savings was $106.18 every 90 days.

As shown in both Canadian and international settings, medication cost affects compliance.[15,16] Populations of lower socioeconomic status, such as patients with PAD, are more vulnerable to this factor. Given that Canadian per capita expenditures on prescription medications rank among the highest in the world, second only to those in Switzerland,[17] we need to recognize the importance of strategically selecting medical therapies to limit patient cost and promote adherence. Reduction of expenditures on prescription medications may further result in system-level efficiencies, such as reductions in insurance costing and other consumer expenses, which, in turn, may further improve adherence.

Although concern may be raised regarding the interchangeability of generic and brand-name medications, a systematic review and meta-analysis showed the lack of significant difference in efficacy between these 2 groups.[18] In light of this and the substantial cost disparity observed in the present study, it is difficult to justify continued prescription of brand-name agents, particularly in populations of low socioeconomic status.

Table 3. Cost range for 90-day prescriptions, not including dispensing fee*

	Generic		Brand name	
Drug class	Cost rage, $	Cost variation, $	Cost range, $	Cost variation, $
Angiotensin-converting-enzyme inhibitors				
Enalapril	25.73–74.01	48.28	134.64–411.03	276.39
Lisinopril	26.00–76.01	50.01	96.93–747.00	650.07
Perindopril	27.52–52.01	24.49	89.01–363.39	274.38
Ramipril	7.94–65.17	57.23	83.55–264.03	180.48
Trandolapril	22.44–56.45	34.01	87.90–150.00	62.10
Angiotensin receptor blockers				
Candesartan	22.17–48.45	26.28	138.93–399.72	260.79
Valsartan	15.54–61.01	45.47	125.79–452.70	326.91
Antiplatelet agents				
ASA	10.35–21.90	11.55	16.35–66.57	50.22
Clopidogrel	25.57–59.41	33.84	271.74–384.03	112.29
Direct factor Xa inhibitor				
Rivaroxaban, 2.5 mg twice daily	NA	—	129.15–174.66	45.51
Statins				
Atorvastatin	23.19–45.21	22.02	246.03–348.30	102.27
Rosuvastatin	19.71–50.16	30.45	198.03–291.03	93.00

ASA = acetylsalicylic acid; NA = not applicable.
*Cost represents that of the maximum evidence-based dosage of each drug, except that the enalapril dosage was 10 mg twice daily (the American College of Cardiology guideline's maximum dosage is 20 mg twice daily, but only for patients categorized as New York Heart Association Functional Class IV[12]), and the rivaroxaban dosage was 2.5 mg twice daily, in keeping with the COMPASS regimen therapy.[14]

Table 4. Lowest- and highest-cost regimen for a 90-d supply of guideline-based[12] medical therapy, including dispensing fee

	Lowest-cost regimen		Highest-cost regimen	
Variable	Drug	90-d cost, $	Drug	90-d cost, $
Drug class				
Angiotensin-converting-enzyme inhibitors	90-d ramipril (generic)	11.83	30-d lisinopril (brand-name)	779.97
Antiplatelet agents	90-d ASA (generic)	10.35	30-d clopidogrel	384.03
Direct factor Xa inhibitors	90-d rivaroxaban (brand-name)	129.15	NA	—
Statins	90-d rosuvastatin (generic)	19.71	90-d atorvastatin (brand-name)	384.30
Potential cost savings, $				
Total quarterly cost		171.04		1548.30
Potential quarterly savings		1377.26		—
Total monthly cost		57.01		516.10
Potential monthly savings		459.09		—

ASA = acetylsalicylic acid; NA = not applicable.

With regard to cost differences based on dispensing institution, our results suggest that chain pharmacies provide the lowest dispensing fees to consumers. However, this may reflect differences in services and counselling provided by each service location. Further investigation is required to better understand this disparity.

The combination of low-dose rivaroxaban (2.5 mg twice daily) and ASA reduces rates of major adverse cardiac and limb events (including major amputation) in patients with PAD while maintaining an acceptable bleeding profile.[14] Cost is a barrier to using this combination, with 70% of vascular surgeons in a Canadian survey citing cost as their principal concern with direct oral anticoagulant prescribing.[19] Our study shows that the combination of low-dose rivaroxaban and ASA remains less expensive than brand-name Plavix (Bristol-Myers Squibb Pharmaceutical Group) monotherapy, although it is more expensive than generic clopidogrel. Regardless, given the proven efficacy of low-dose rivaroxaban and ASA, we do not believe that these cost differences should drive clinical decision-making.

Ultimately, the variability in pharmacy pricing shows the utility of collective bargaining through a national pharmaceutical care plan.[20] Our findings show that the net cost savings achievable through such a program would be

Table 5. Lowest- and highest-cost regimen for a 90-day supply of guideline-based[12] medical therapy, generic drugs only, including dispensing fee

	Lowest-cost regimen		Highest-cost regimen	
Variable	Drug	90-d cost, $	Drug	90-d cost, $
Drug class				
Angiotensin-converting-enzyme inhibitors	90-d ramipril (generic)	11.83	30-d lisinopril (generic)	76.01
Antiplatelet agents	90-d ASA (generic)	10.35	30-d ASA (generic)	21.90
Direct factor Xa inhibitors	90-d rivaroxaban (brand-name)	129.15	30-d rivaroxaban (brand-name)	129.15
Statins	90-d rosuvastatin (generic)	19.71	30-day rosuvastatin (generic)	50.16
Potential cost savings, $				
Total quarterly cost		171.04		277.22
Potential quarterly savings		106.18		—
Total monthly cost		57.01		92.41
Potential monthly savings		35.40		—

ASA = acetylsalicylic acid.

substantial and, given the documented effect of cost on medication adherence,[15,16] would almost certainly improve patient outcomes.

In addition to the strategies that we outline, other potential cost-saving measures warrant consideration to optimize patient drug costing. These include options such as pill splitting to minimize cost, and system-level interventions such as the involvement of interdisciplinary care partners, including social work and family health team navigators, aimed at identifying potential drug coverage plans that patients may be eligible for. In addition, multiple jurisdiction-specific electronic resources have been developed to facilitate improved dissemination of cost differences among dispensers and available coverage options (Appendix 2, available at www.canjsurg.ca/lookup/doi/10.1503/cjs.003722/tab-related-content).

Limitations

We assumed that all drugs within a class provide equivalent effect, with the exception of antithrombotics.[12] In addition, cost variations may differ in provinces other than those sampled, as well as in other communities, such as rural or First Nations, and may vary over time; health care providers may need to assess costs in their own community.[21] The disparities illustrated here represent potential cost savings only. The actionability of these differences is dependent on current prescribing practices, assessment of which was outside the scope of this study.

Although this study specifically assesses prescribing of vascular protective medication, it is important to consider that medication expenses for comorbid conditions, such as diabetes, which are common in PAD populations, likely compound prescribing disparities and result in substantial additional excess cost. Medication costing should continue to be taken into consideration when optimizing these comorbidities. In addition, barriers to medication adherence are multifactorial and likely include barriers at the patient, prescriber and system levels. Additional strategies such as polypill designs to reduce pill burden may further improve adherence rates.[22]

Conclusion

By opting for prescriptions for 90 days or as long as possible, selecting the lowest-cost generic drugs available in each drug class and identifying dispensing locations with lower fees, prescribers can minimize out-of-pocket patient medication expenses. Minimizing out-of-pocket medication costs may help improve adherence to guideline-recommended therapies for the secondary prevention of vascular events in patients with PAD.

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References

1. Song P, Rudan D, Zhu Y, et al. Global, regional, and national prevalence and risk factors for peripheral artery disease in 2015: an updated systematic review and analysis. *Lancet Glob Health* 2019;7:e1020-30.
2. Fowkes FGR, Rudan D, Rudan I, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet* 2013;382:1329-40.
3. Bhatt DL, Steg PG, Ohman EM, et al. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA* 2006;295:180-9.
4. Armstrong EJ, Chen DC, Westin GG, et al. Adherence to guideline-recommended therapy is associated with decreased major adverse cardiovascular events and major adverse limb events among patients with peripheral arterial disease. *J Am Heart Assoc* 2014;3:e000697.
5. Anand SS, Kundi A, Eikelboom J, et al. Low rates of preventive practices in patients with peripheral vascular disease. *Can J Cardiol* 1999;15:1259-63.
6. Kundhal KK, Chin SL, Harrison L, et al. Patterns of medical therapy in patients with peripheral artery disease in a tertiary care centre in Canada. *Can J Cardiol* 2007;23:357-61.
7. Welten GMJM, Schouten O, Hoeks SE, et al. Long-term prognosis of patients with peripheral arterial disease: a comparison in patients with coronary artery disease. *J Am Coll Cardiol* 2008;51:1588-96.
8. Smolderen KG, Bell A, Lei Y, et al.; REACH registry investigators. One-year costs associated with cardiovascular disease in Canada: insights from the REduction of Atherothrombosis for Continued Health (REACH) registry. *Can J Cardiol* 2010;26:297-305.
9. Pande RL, Perlstein TS, Beckman JA, et al. Secondary prevention and mortality in peripheral artery disease: National Health and Nutrition Examination Study, 1999 to 2004. *Circulation* 2011;124:17-23.
10. Pande RL, Creager MA. Socioeconomic inequality and peripheral artery disease prevalence in US adults. *Circ Cardiovasc Qual Outcomes* 2014;7:532-9.
11. McIntyre WF, Belesiotis P, McClure GR, et al. Strategies to reduce out-of-pocket medication costs for Canadians living with heart failure. *Cardiovasc Drugs Ther* 2021;35:1009-23.
12. Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2017;135:e686-725.
13. *Table: 11-10-0239-01 (formerly CANSIM 206-0052): Income of individuals by age group, sex and income source, Canada, provinces and selected census metropolitan areas*. Ottawa: Statistics Canada; 2018, modified March 13, 2023. Available: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1110023901 (accessed 2020 July 23).
14. Anand SS, Bosch J, Eikelboom JW, et al.; COMPASS Investigators. Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease: an international, randomised, double-blind, placebo-controlled trial. *Lancet* 2018;391:219-29.
15. Musich S, Cheng Y, Wang SS, et al. Pharmaceutical cost-saving strategies and their association with medication adherence in a Medicare Supplement population. *J Gen Intern Med* 2015;30:1208-14.
16. Persaud N, Bedard M, Boozary AS, et al.; Carefully Selected and Easily Accessible at No Charge Medicines (CLEAN Meds) Study Team. Effect on treatment adherence of distributing essential medicines at no charge: the CLEAN Meds randomized clinical trial. *JAMA Intern Med* 2019;180:27-34.
17. Morgan SG, Leopold C, Wagner AK. Drivers of expenditure on primary care prescription drugs in 10 high-income countries with universal health coverage. *CMAJ* 2017;189:E794-9.
18. Kesselheim AS, Misono AS, Lee JL, et al. Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. *JAMA* 2008;300:2514-26.
19. McClure GR, Kaplovitch E, Chan N, et al. A national Canadian survey of antithrombotic therapy following urgent and emergent limb revascularization. *Can J Cardiol* 2021;37:504-7.
20. Canada needs universal pharmacare [editorial]. *Lancet* 2019;394:1388.
21. Anand SS, Abonyi S, Arbour L, et al. Explaining the variability in cardiovascular risk factors among First Nations communities in Canada: a population-based study. *Lancet Planet Health* 2019;3:e511-20.
22. Yusuf S, Joseph P, Dans A, et al.; International Polycap Study 3 Investigators. Polypill with or without aspirin in persons without cardiovascular disease. *N Engl J Med* 2021;384:216-28.