

Economic analysis of an integrated virtual health care model targeting medication- related problems for high-risk chronic kidney disease patients in Ontario, Canada

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Abstract

Background/Objectives

: Adverse drug events (ADEs) pose increasing risks for patients with chronic kidney disease (CKD). Integrated virtual care models that leverage clinical pharmacist expertise may mitigate these risks, yet evidence on their economic value remains limited. This study evaluates the implementation costs, avoided health system resource use, and return on investment (ROI) of an integrated virtual pharmacy (iVRx) program for CKD patients.

Methods

A retrospective cost and ROI analysis was conducted using referrals to the iVRx program from February 1, 2021, to January 31, 2022, across nephrology clinics at the University Health Network in Ontario, Canada. pharmacist–patient encounters and overall program implementation. Avoided health system utilization attributable to pharmacist-identified medication-related problem interventions was estimated, including primary care visits, specialist visits, emergency department (ED) visits, and hospital admissions. ROI was calculated as health system costs averted relative to total program costs.

Results

A total of 80 referrals in the iVRx program were reviewed during the 12 month observation period. Participants were 58 years old (+/- 17) (69% males with a mean (SD) of 8 (+/-3) medications and 6 (+/-3) co-morbidities). The total cost of program implementation was \$9,253.81 for 387 health services provided (cost per person of \$115.67). Early interventions to address identified medication-related problems in patients in the iVRx program resulted in averting a total of 61 health system resource use events, which included 6 primary care, 37 specialist, 15 ED visits, and 3 hospital admissions, which was associated with a total cost of \$75,231.27. Across all scenarios, the iVRx program achieved an approximate ROI of \$8 for every \$1 invested.

Conclusions

This is the first study to estimate the ROI of an integrated virtual care model targeting ADEs in high-risk patients with chronic kidney disease (CKD). The results of this study provide evidence of economic benefits in CKD patients, demonstrating that the costs of implementing the iVRx outweigh the monetized benefits of the intervention. Future studies should assess actual health system resource use in CKD patients using an integrated virtual health care model through randomized controlled trials or evaluation of health administrative datasets.

Article Summary

Strengths and Limitations

- Evaluates the potential economic return on investment of a virtual outpatient pharmaceutical care program supporting individuals living with chronic kidney disease
- Characterizes healthcare resource utilization and costs that could be averted with the integration of comprehensive pharmacy services into the care pathway

- Recruitment was from an urban subspecialty clinic, with participants potentially more likely to be tech savvy than the general CKD population, possibly increasing the digital equity divide
- Observational single-center analysis from a quaternary teaching center and a specialty pharmacy evaluating theoretically adjudicated outcomes

Background

Adverse drug events (ADEs), now a third leading cause of death in the US, (1) stem from a larger issue of medication-related problems (MRPs). MRPs account for the top five leading causes of death in patients with complex chronic diseases like chronic kidney disease (CKD) due to complex care prescriptions leading to frequent medication non-adherence, adverse drug events, and poor clinical outcomes.(2, 3) These MRPs not only threaten patient safety and poor clinical outcomes but also impose substantial costs on healthcare systems.(4–6) Despite global calls to action by the World Health Organization (WHO) in 2017 to address rising MRPs, it continues to be a growing global public health burden, resulting in annual emergency department (ED) visits of 96,925 and 1.3 million deaths in the US alone. (7) In Canada, ADEs pose similar health system and economic burdens, resulting in national costs exceeding \$13 billion CAD annually.(8, 9) There is a dire need for targeted models of care to address the escalating crisis of medication-related problems (MRPs). With their specialized expertise in medication management, pharmacists are well-positioned to identify and resolve such issues; however, their integration into clinical teams and patient care pathways remains inconsistent, limiting their potential impact.(10)

Recent evidence suggests that embedding pharmacists within healthcare teams can significantly improve patient outcomes and generate meaningful cost savings, especially when pharmacists are positioned to proactively address medication-related challenges.(11) In CKD, this evidence is more prominent.(12) Barriers to optimal integration have been cited, including gaps in communication and appropriate medication information transfer, a lack of standardized follow-up and monitoring, and pharmacy services being delivered in siloes.

To address these gaps, in 2021, the University Health Network's (Toronto, Canada) Division of Nephrology implemented a virtual pharmacy program (iVRx) integrating community pharmacists to deliver a targeted intervention in partnership with McKesson Canada. The iVRx aims to ensure access, standardized follow-up and monitoring, communication between all clinicians, and bidirectional transfer of pertinent medication-related information aligned with pharmacy practice standards for outpatient nephrology care. (13) The initial evaluation of the program demonstrated that identifying MRPs enabled early interventions to prevent further patient harm.(14) The continued implementation and sustainability of integrated care models with targeted medication reviews rely on ongoing financial resources. This study evaluates the integrated virtual pharmacy program designed for patients with CKD, focusing on its effectiveness in identifying and resolving MRPs, and its impact on health care resource utilization and costs. By conducting a cost and return on investment (ROI) analysis, we aim to determine whether integrating pharmacy services can deliver both health system and financial benefits, and to understand the implementation costs to support broader adoption and reimbursement of such models within the healthcare system.

The overarching goal was to perform an economic evaluation to determine the cost of the integrated virtual health care model and its implementation. More specifically, the objectives of this study were to: 1) Identify the cost of the health services provided (*descriptive cost analysis of health services*)

2) Assess health system resource use, including primary care, specialist visits, ED visits, and hospitalizations (*descriptive cost analysis of health system resource use*)

3) Determine the return on investment (ROI) associated with the implementation of iVRx in patients with chronic kidney disease (*return on investment analysis*)

Methods

Study Design

This study is an economic analysis based on a retrospective review of referrals received in the iVRx program from February 1, 2021, to January 31, 2022 (12-month period). This study is based on descriptive costing and return on investment analysis. The analysis was conducted in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement (15) while following the Canadian Agency for Drugs and Technologies in Health (CADTH) (16) guidelines for economic evaluation in Canada. The University Health Network institutional research ethics board approved the study (**IRB number:21-6180**). Human ethics and consent to participate in the study has been waived.

Study setting and population

iVRx was implemented at the University Health Network (UHN) Nephrology Division's ambulatory clinics (Toronto, Ontario, Canada), which partnered with McKesson Canada's Pharmacy division (specialty pharmacy and online retail pharmacy). The iVRx program launched on February 1, 2021, in the five target clinics (Comprehensive Cardio-Renal-Endo (CaRE) - cardiovascular renal and metabolic syndrome, OncoNephrology, and Glomerulonephritis clinics). The Division of Nephrology at UHN is an academic centre comprising 23 nephrology practices, offering services ranging from general nephrology to subspecialty clinics, dialysis, and transplantation, and seeing over 4000 ambulatory nephrology outpatient visits per year throughout the province of Ontario.

Eligible adult (> 18 years of age) patients were those residing in Ontario from the five nephrology clinics who presented with a new prescription for any medication in one of four targeted classes (sodium glucose transport cotransporter 2 (SGLT-2) inhibitors, glucose-like peptide 1 (GLP-1) agonists, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, or immunosuppressants). All consecutive patient referrals could enroll regardless of language, ethnicity, or access to digital technology, if the patient or caregiver had access to a primary telephone. Those who had medically documented cognitive impairment, lived in a long-term care facility, taking less than 2 prescription medications or were unavailable for extended periods of time were not referred into the program.

Intervention

Nephrologists initiated enrollment in the iVRx program by using a digital referral form and prescription.(14) Pharmacists contacted the patient within 24 hours of receiving the prescription for a baseline call. The baseline call included a standardized medication review (medication reconciliation, drug reimbursement navigation, education, adherence check, and setting up a tailored monitoring plan). The monitoring plan provided succinct parameters for pharmacists to check at specific time points: one week after delivery, then one month, and three months. Scheduled follow-up visits included adherence checks, side-effect investigations, and changes in clinical outcomes. All consultations with the patient or caregiver were conducted with telephone or video call preapproved platforms (Microsoft Teams). Pharmacists then connect and collaborate with the prescribers by sharing patient status reports and issues with each baseline and follow-up call with specific action items and next steps.

Data Collection

Study perspective and Time Horizon

The study used a payer perspective, considering the Ontario Ministry of Health and Long-Term Care (MOH) as the payer for health services, specifically physician visits, emergency department visits, and hospital admissions. We considered the lifetime of the iVRx intervention period (up to 12 months). In line with CADTH guidelines, we did not consider a 1.5% discount rate as there were no costs and consequences beyond 1 year. Descriptive statistics were summarized for all costs. All costs are reported in 2025 Canadian dollars (Can\$) using the Bank of Canada Consumer Price Index for inflation to a given base year.⁽¹⁷⁾

Baseline characteristics of study participants were summarized using descriptive statistics. Continuous variables were summarized as mean $\pm$ standard deviation (SD) or median and interquartile range (IQR), as appropriate, and categorical variables were summarized by counts and frequencies.

Cost analysis of health services provided and total program cost

Costs for the iVRx program obtained from the retrospective review of referrals considered the following: number of pharmacist-patient encounters (number baseline calls, standard follow up calls, email correspondence and additional phone calls), documented pharmacist time spent per encounter, and average pharmacist salary (expressed as hourly wage based on mid-career 2025 Ontario community pharmacist).⁽¹⁸⁾ Non-labor costs were not included as they were operational prior to the implementation of iVRx. A pharmacist-patient encounter counted as a health service provided, and the cost was validated using the Ontario MedsChek Professional Services guidebook as a reference point.⁽¹⁹⁾ The total cost of iVRx's implementation and the cost per patient considered the number of pharmacist-patient encounters (health services provided) throughout the intervention.

Cost analysis of health care system resource use

The consequence from the health service provided (pharmacist-patient encounter) included the avoided health care system use secondary to each pharmacist-patient encounter. The health care system use avoided was identified based on an adjudication process. Specifically, the adjudication process started with assessing documented medication-related problems identified from each pharmacist-patient encounter. Medication-related problems (MRPs) defined as "any events or circumstances that involves drug therapy that actually or potentially interferes with the desired health outcomes" and "issues related to: obtaining, taking, managing effects and communication or coordination related to medications, including insufficient information about medications"⁽²⁰⁾ were documented in the standard clinical notes for each patient and encounter. All documented MRPs were independently categorized for their clinical severity (mild, moderate, severe) by individual registered pharmacists (SO, KC, KL, JMB) guided by the National Coordinating Council for Medication Error Reporting and Prevention Index.^(21, 22) Moderate and severe MRPs were further adjudicated on the potential health care system used if the intervention was not implemented (e.g. no incremental healthcare utilization, result in a primary care visit, specialist visit, ED or hospitalization). Where the adjudicated outcome differed between the raters, consensus was reached by discussing each MRP and the patient documented encounter information to arrive at a consensus.

The descriptive cost analysis of health system resource use included the costs associated with primary care, specialist, ED visits and hospital admissions. Due to limitations of the available published data specific to the cost of ED visits for CKD patients, we assumed that the cost of an ED visit for CKD patients enrolled in the study would be in line with the cost of an ED visit for a complex patient, e.g. those of a heart failure patient.^(23, 24) For the base case

scenario regarding nephrologists billing costs, we considered the average value of A165 (\$162.90) and A160 (\$310.45).(25) The average of the two values was considered as there may be differences in service fee depending on whether it is a solo nephrologist or a multidisciplinary clinic providing care.

Return on investment (ROI) analysis

To calculate the iVRx ROI, the benefit or return of an investment, which is the cost of the averted health system use or gains of iVRx, was divided by the cost of the investment of iVRx. The ROI was expressed as dollars saved, and a percentage.(26, 27) The iVRx ROI formula is described in Fig. 1. We considered that an ROI greater than or equal to 1 signifies the returns generated by improvement actions, such as the iVRx intervention, are greater than or equal to the costs for the development and implementation of the intervention; hence, this ROI is considered to be positive. If the ROI were less than 1, implementing iVRx would yield a net loss from changes in quality and health care utilization. In this case, the ROI would be considered to be negative.(28) We acknowledge that while the term good ROI remains subjective, many professionals consider a good ROI to be 10.5% or greater for investments in stocks. This number is the standard because it is the average return of the Standard and Poor's 500 (S&P 500),(29) a stock market index tracking the stock performance of 500 of the largest companies listed on stock exchanges in the United States. Currently, the S&P 500 index serves as a benchmark of the overall performance of the U.S. stock market. Hence, for the purpose of the ROI analysis in this study, we considered a 10.5% ROI or greater to indicate a very good ROI.

We ran a sensitivity analysis of the ROI for low and high values of the spectrum associated with nephrologists and specialist care, informed by expert consultation to reflect real-life care scenarios appropriately.

Patient and public involvement in the design and implementation of study was not possible due to the nature of the retrospective chart reviews.

Results

Study population

A total of 80 referrals were received and assessed from February 1, 2021, to January 31, 2022. Of the 80 referrals, 46 patients received baseline plus 3 calls, 13 patients received only the baseline call, and one patient required an additional follow-up at 6 months. Table 1 summarizes the primary causes of CKD and the baseline characteristics. The majority of participants were male (69%), and the mean age (SD) was 58+/-17 years. Most (92%) had a mean number of comorbidities 6+/-3. The median number of medications at referral was 8 [8,11].

Table 1
Patient Characteristics

Variable	n = 80
Age (years)	57.7 (+/-17.3)
Mean (STD)	60 [47,70]
Median [IQR]	31 (39%)
Age Categories	18 (23%)
18 to 55	16 (20%)
55–64	15 (19%)
65–74	
≥ 75	
Men (n%)	55 (69%)
Medications	8 (+/-3)
Mean (STD)	8 [8,11]
Median [IQR]	3 (4%)
Number of Medications (n = 72)	14 (19%)
Less than 3	36 (50%)
3 to 5	19 (26%)
6 to 10	
Greater than 10	
Cause of CKD (n)	35
Diabetic kidney disease	10
IgA nephropathy	10
Cancer	7
Membranous glomerulopathy	5
Focal Segmental glomerulosclerosis	3
Hypertension	3
Drug induced toxicity	1
SLE	1
Hereditary kidney disease	1
Obstructive uropathy	4
Other	
Comorbidities	6 (+/-3)
Mean (STD)	6 [4,8]

Variable	n = 80
Median [IQR]	
Comorbidities (n)	69
Cardiovascular Conditions	47
Endocrine and Metabolic Conditions	25
Respiratory Conditions	24
Gastrointestinal Conditions	23
Cancer	16
Musculoskeletal Conditions	10
Blood Disorder	6
Neurological Conditions	6
Psychiatric Conditions	

Costs

Health services provided and total program cost

The iVRx program delivered 80 baseline calls, followed by a total of 63 follow up calls, with 54 call #1, 43 call #2, 43 #3, and one call #4. The team delivered an additional 115 phone calls outside of the standard baseline and follow-up calls. In total, 387 health services provided (pharmacist-patient encounters) to iVRx patients with total implementation cost of \$9,253.81 (\$115.67 cost/patient). (Table 2)

Table 2
Costs of health services provided by iVRx program

Health services (Pharmacist-patient encounter)	Total (n)	Cost per Unit ^a	Total cost
Baseline Call*	80	\$51.97	\$4,157.6
Follow up			
Call 1	63	\$17.32	\$1,091.16
Call 2	54		\$935.28
Call 3	43		\$744.76
Call 4	1		\$17.32
Other call	115		\$1,991.8
Email	31	\$10.19	\$315.89
Total	387		\$9,253.81
Total cost per patient			\$115.67
^a Cost in 2025 Can\$			
*Assumption: Baseline call took approximately 1 hour			

Health care system resource use and associated cost

Eighty potential health system resource use was averted with the iVRx interventions made on identified medication-related problems. Specifically, the potential health care system use avoided included 6 primary care visits, 37 specialist visits, 15 ED visits and 3 hospitalizations. The total costs associated with the respective health system use were \$904.2 for primary care visits, \$11,486.65 for specialist visits, \$12,198.15 for ED visits and \$53,371.95 for hospitalizations. The total cost associated of health system use averted was \$77,960.95. (Table 3)

Table 3
Healthcare system resource averted and associated cost

Healthcare System Resource	Total averted (n)	Base Case		Sensitivity Analysis Low value		Sensitivity Analysis Higher value	
		Cost ^a per unit HSU*	Total Cost	Cost per unit HSU	Total Cost	Cost per unit HSU	Total Cost
Primary care visit	6	\$150.70	\$904.20	\$150.70	\$904.20	\$150.70	\$904.20
Specialist visit	37	\$236.67	\$8,756.97	\$162.9	\$6,027.3	\$310.45	\$11,486.65
Emergency visit	15	\$813.21	\$12,198.15	\$813.21	\$12,198.15	\$813.21	\$12,198.15
Hospitalization	3	\$17,790.65	\$53,371.95	\$17,790.65	\$53,371.95	\$17,790.65	\$53,371.95
Total	61		\$75,231.27		\$72,501.63		\$77,960.95
* HSU - healthcare system use							
^a Cost reported in 2025 Canadian dollars (Can\$)							

Return on investment (ROI)

Base case scenario

The overall cost of the iVRx implementation was \$9,253.81. The total cost of health system use averted by iVRx’s interventions was \$75,231.27. Based on the gains over costs of the iVRx implementation, the corresponding ROI of iVRx was \$8.13 for every dollar invested in the program.

Sensitivity analysis

Based on the gains over costs of the iVRx implementation, the corresponding ROI of iVRx was \$7.83 (lower value) and \$8.42 (higher value) for every dollar invested in the program.

Discussion

In this study, we found that CKD patients enrolled in the iVRx program, a comprehensive integrated virtual pharmacy service, intervened on MRPs, possibly avoiding adverse drug events. Our results demonstrated that these clinically relevant MRPs required an intervention to prevent patient harm. Furthermore, these interventions potentially averted a significant health care cost avoiding unnecessary visits to the general practitioner, specialist, emergency room, or hospitalizations. We note that the corresponding ROI of iVRx was an estimated eight-fold potential benefit in averted

healthcare system resource use for every dollar invested in the iVRx program. The study highlights the cost-effectiveness of a virtual integrated care model harnessing pharmacist expertise in addressing MRPs, its impact on health care resource use and translating to a favorable ROI to address significant burden of MRPs in vulnerable patients with CKD.

Several factors may account for the substantial impact observed in the study findings. First, the iVRx program employs an integrated model designed to address critical barriers in the medication management process—specifically, communication, monitoring, and access.⁽³⁰⁾ The implementation of a unified communication channel and a consolidated referral/prescription form effectively streamlines the transfer of medication-related information among clinicians, thereby mitigating inefficiencies and reducing the risk of miscommunication. Notably, deficiencies in communication between patients and healthcare providers are a leading cause of adverse drug events (ADEs), with over 50% of preventable ADEs in ambulatory care attributed to inadequate exchange of medication information.⁽³¹⁾ Furthermore, the program incorporates a standardized follow-up and monitoring protocol that proactively identifies medication-related problems (MRPs) in vulnerable patients with chronic kidney disease (CKD). Evidence suggests that insufficient patient-clinician communication, or patients' inability to articulate medication concerns, contributes to more than half of preventable adverse drug reactions (ADRs), with approximately 36% of MRPs occurring during the monitoring phase.⁽⁷⁾ The model strategically positions pharmacists to effectively address MRPs by providing them with the right tools for communication and effective monitoring. Furthermore, using a virtual health space broke down siloed practices between health care professionals (e.g., physicians and pharmacists), allowing the virtual platform to open a virtual corridor to support interprofessional collaboration between clinicians. The model does not rely on elaborate and resource-intensive solutions but instead harnesses readily available processes, expertise, and digital solutions without large, extensive system overhauls. With this, the solution is not resource-intensive nor pulls further from an already strained health care system.

A second factor that may underlie the substantive benefits reported in this analysis is the targeting of high-risk patients and the delivery of services where they are needed the most.⁽³²⁾ The WHO identified patients with a high number of comorbidities and medications vulnerable to MRPs.⁽⁷⁾ The frequency of health care visits, transitions of care, and providers further increases this risk. In Ontario, Canada, a study of the annual MedsCheck program showed that less than 5% of eligible patients with diabetes received follow-up and monitoring.⁽³³⁾ and the majority were conducted in younger patients with fewer medications rather than high-risk patients. Through the iVRx program, community pharmacists are supported by focusing their expertise towards patients who will benefit the most; thus effectively providing impactful service.

Challenges with sustainability and reimbursement exist for this virtual pharmacist-led clinical care, which we have demonstrated provides a reasonable return-on-investment (ROI) to avert more costly healthcare resource utilization. Suppose chronic disease management programs like this are to exist with a pharmacist providing chronic disease management care. In that case, there is a need to reassess *pharmacist* service (not necessarily pharmacies) reimbursement model in Ontario and Canada that is independent of the dispensing of medication and aligned with the outpatient and/or community setting. Insufficient reimbursement for pharmacist chronic disease management care activities for individuals with diabetes has been identified as one of the barriers to providing routine monitoring and follow-up in a community setting.⁽¹⁰⁾ For this patient population, more than half of the individuals are not necessarily eligible for public health coverage for medications (Ontario Drug Benefit), and thus their care is covered with private insurance; however, limited chronic disease management reimbursement exists in the private insurance space for pharmacists. Provincial reimbursement in Ontario for MedsCheck and Minor Aliment reimbursement in Ontario is a step in the right direction; however, the intervention does not align with chronic disease management frequency of care. Reimbursement for pharmacists' care in these patients with complex needs should be aligned with

the pharmaceutical care standards of practice for patients with CKD.(13, 34) Provincial pharmacy programs for the CKD patient population have been implemented with dedicated funding to support care elsewhere in Canada.(10, 32) Findings in the current study demonstrate that the positive ROI emphasizes the need for further investment in the pharmacy-provided services, which is a significant opportunity for policy change to address the financial burden of these high risk patients.

Finally, to the best of our knowledge, this is the first study to demonstrate interventions delivered through an integrated pharmacy model that can potentially avoid health care system use and result in an \$8.13 return on investment for every \$1 spent on the program. This is especially significant in patients with CKD, where medication management is complex, MRPs are high, and the financial burden to the health care system is costly.(5) In Canada, managing advanced chronic kidney disease carries an estimated cost of care of \$14,634 per year per patient.(4) Comparably, an analysis of advanced CKD without renal replacement therapy in the US showed a cost of \$11,879 for general outpatient management escalating to \$31,212 for an acute hospitalization from a CKD-related complication (e.g., hyperkalemia), similar to the current study's population.(35) The rise in downstream health care system costs is in part a consequence of unaddressed MRPs in vulnerable CKD patients. Recently, the URGEIM trial in France (36) demonstrated similar results in decreasing ED visits when solutions integrate the expertise of pharmacists and position them within in the circle of care. Weber et al (37) studied a multidisciplinary care model in patients with cardio-renal metabolic syndrome, demonstrating a projected \$250 million USD cost savings, while Vassalotti et al's (38) advanced CKD study showed both a decrease in health care system use and cost savings. Though results from these types of studies are limited, they provide a promising start to demonstrate the impact of integrated care models to address MRPs in complex chronic diseases like CKD on improvements in health care use and costs.

The present study has some limitations. First, there is no data on how frequently individuals referred to the iVRx program used the health care system after each pharmacist intervention was captured. Also, MRPs and interventions were only categorized by their potential for patient harm and subsequent health care use, a process measure, and not actual ADEs. A rigorous adjudication process by independent pharmacists was followed to ensure classification followed a standardized, globally accepted methodology, thereby strengthening the agreement to practice standards. (21) A study to relate actual ADEs to health resource outcomes or clinical events would require a larger study of longer duration. Additionally, there may be concerns about the generalizability of the study's findings in that the referrals came from one quaternary urban academic centre. As patients were referred from five different nephrology clinics, we anticipate that a broad range of patients with complex chronic diseases will be fully represented in the study, reflecting the current population. Finally, using only one corporate community pharmacy partner may limit the practice's applicability and scalability to other community pharmacies. However, the proposed model harnessed current standards of practice and resources, without requiring large deviations or a process overhaul, to support its feasible implementation alongside other community pharmacy practices.(39)

Conclusion

The findings illustrate the economic benefits of iVRx intervention in CKD patients. This is the first evaluation estimating the ROI of the integrated virtual health care (iVRx) intervention for CKD patients in Ontario, demonstrating that the costs to implement iVRx are outweighed by the monetized benefits of the intervention. There is a need to implement targeted integrated care models to address the increasing burden of MRPs in patients with complex chronic disease. Strategies need to ensure they are cognizant of the limitations of the current health care system and its resource constraints. The present study provides evidence of an integrated care model using pharmacist expertise to address MRPs in complex chronic kidney disease, potentially diverting unnecessary health care use and achieving a positive return on investment.

Declarations

Clinical Trial number: Not Applicable

University Health Network institutional research ethics board (IRB) number: 21-6180

Human Ethics and Consent to Participate declarations: not applicable

Ethics Approvals and consent to participate

Ethics approval was obtained from the Research Ethics Board at the University Health Network (UHN) (IRB:21-6180). Patient consent for this publication is waived by the UHN institutional and research ethics committee. All methods were carried out in accordance with relevant guidelines and regulations. The analysis was conducted in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement while following the Canadian Agency for Drugs and Technologies in Health (CADTH) guidelines for economic evaluation in Canada.

Consent of publication

Not applicable

Data availability statement

Deidentified patient data are available upon reasonable request from the corresponding author Dr. Valeria Rac.

Competing interests and disclosures

CC consults for Medtronic, Quanta and Dialco. CC holds an investigator-initiated grant from Medtronic ERP program.

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Author contributions

All authors participated in the planning, execution or analysis of the study. All have read and approved the final submitted version. All authors vouch for the completeness and accuracy of the data and analyses and for the fidelity of the trial to the protocol and statistical analysis plan, both of which are available on request. The two co-first authors (AS and SO) and last author (VR) led manuscript preparation, drafting and writing. SWO and CC obtained funding and drafted the manuscript. VR and CC are responsible for the overall content as guarantor and accept full responsibility for the finished work, the conduct of the study, had access to the data, and controlled the decision to publish.

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References

1. Rodziewicz TL, Houseman B, Vaqar S et al. Medical Error Reduction and Prevention. [Updated 2024 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK499956/>
2. Le Louët H, Pitts PJ. Twenty-First Century Global ADR Management: A Need for Clarification, Redesign, and Coordinated Action. *Ther Innov Regul Sci*. 2023;57(1):100–3.
3. Bourgeois FT, Shannon MW, Valim C, Mandl KD. Adverse drug events in the outpatient setting: an 11-year national analysis. *Pharmacoepidemiol Drug Saf*. 2010;19(9):901–10.
4. Manns B, Hemmelgarn B, Tonelli M, Au F, So H, Weaver R, et al. The Cost of Care for People With Chronic Kidney Disease. *Can J Kidney Health Dis*. 2019;6:2054358119835521.
5. Levin A, Chaudhry MR, Djurdjev O, Beaulieu M, Komenda P. Diabetes, kidney disease and cardiovascular disease patients. Assessing care of complex patients using outpatient testing and visits: additional metrics by which to evaluate health care system functioning. *Nephrol Dial Transpl*. 2009;24(9):2714–20.
6. Arnold SV, Kosiborod M, Wang J, Fenici P, Gannedahl G, LoCasale RJ. Burden of cardio-renal-metabolic conditions in adults with type 2 diabetes within the Diabetes Collaborative Registry. *Diabetes Obes Metab*. 2018;20(8):2000–3.
7. World Health Organization. Integrated Health Services (ISH) MWH. Global burden of preventable medication-related harm in health care: a systematic review. 2024 March 7 2024. [Available from: <https://www.who.int/publications/i/item/9789240088887>] Last accessed: January 12, 2026.
8. Wu C, Bell CM, Wodchis WP. Incidence and economic burden of adverse drug reactions among elderly patients in Ontario emergency departments: a retrospective study. *Drug Saf*. 2012;35(9):769–81.
9. Provincial Health Services Authority TUoBC. Canadian Pharmacogenomics Network for Drug Safety: Adverse Drug Reactions. [Available from: <https://cpnds.ubc.ca/about/>] Last accessed: January 12, 2026.
10. MacCallum L, Mathers A, Kellar J, Rousse-Grossman J, Moore J, Lewis GF, et al. Pharmacists report lack of reinforcement and the work environment as the biggest barriers to routine monitoring and follow-up for people with diabetes: A survey of community pharmacists. *Res Social Adm Pharm*. 2021;17(2):332–43.
11. Price E, Shirtcliffe A, Fisher T, Chadwick M, Marra CA. A systematic review of economic evaluations of pharmacist services. *Int J Pharm Pract*. 2023;31(5):459–71.
12. Zafar R, Rehman IU, Shah Y, Ming LC, Goh KW, Suleiman AK, et al. Impact of pharmacist-led intervention for reducing drug-related problems and improving quality of life among chronic kidney disease patients: A

- randomized controlled trial. PLoS ONE. 2025;20(2):e0317734.
13. Cardone KE, Maxson R, Cho KH, Davis JM, El Nekidy WS, Kane-Gill SL, et al. Pharmacy Practice Standards for Outpatient Nephrology Settings. *Kidney Med.* 2022;4(8):100509.
 14. Ong SW, Kitchlu A, Cherney DZI, Leung K, Chan CTM. Virtual Pharmacy: An Integrated Collaborative Redesign Targeting Medication-Related Problems in Patients with Chronic Kidney Disease. *Am J Nephrol.* 2024;55(2):206–13.
 15. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *BMJ.* 2022;376:e067975.
 16. CADTH. Guidelines for the economic evaluation of health technologies. Ottawa. 2025. Available from: <https://www.cda-amc.ca/guidelines-economic-evaluation-health-technologies-canada-4th-edition>. Last accessed: January 12, 2026.
 17. Bank of Canada. Inflation Calculator Ottawa: Bank of Canada. 2025 [26 May 2025]. Available from: <https://www.bankofcanada.ca/rates/related/inflation-calculator/>. Last accessed: January 12, 2026.
 18. Indeed. Pharmacist salary in Ontario 2025 [Pharmacist salary in Ontario]. Available from: <https://ca.indeed.com/career/pharmacist/salaries/Ontario>. Last accessed: January 12, 2026.
 19. Ministry of Health and Long-Term Care. Professional Pharmacy Services Guidebook 3.0. Toronto, ON: Queen's Printer for Ontario. 2016. Available from: <https://files.ontario.ca/moh-medscheck-professional-pharmacy-services-guidebook-2016-07-01.pdf>. Last accessed: January 12, 2026.
 20. Boockvar KS, Santos SL, Kushniruk A, Johnson C, Nebeker JR. Medication reconciliation: barriers and facilitators from the perspectives of resident physicians and pharmacists. *J Hosp Med.* 2011;6(6):329–37.
 21. National Coordinating Council for Medication Error Reporting and Prevention. Types of Medication Errors and Medication Error Index. . Last accessed: January 12, 2026.
 22. Cipolle RJ, Strand LM, Morley PC. Chapter 5. Drug Therapy Problems. In: Cipolle RJ, Strand LM, Morley PC, editors. *Pharmaceutical Care Practice: The Patient-Centered Approach to Medication Management Services*, 3e. New York, NY: The McGraw-Hill Companies; 2012.
 23. Zaour N, Barbeau M, Liu N, Borrelli R, Fischer AA. THE COST OF HOSPITALIZATION AND LENGTH OF STAY FOR CHRONIC HEART FAILURE CASES IN CANADA. *Can J Cardiol.* 2015.
 24. CIHI: High Risk and High Cost. Focus on Opportunities to Reduce Hospitalizations of Dialysis Patients in Canada 2017 [Available from: <https://www.cihi.ca/sites/default/files/document/opportunities-reduce-hospitalizations-dialysis-patients-canada-en.pdf> Last accessed: January 12, 2026.
 25. Ministry of Health. Schedule of benefits. Physicians services under the Health Insurance Act. Toronto, ON: Government of Ontario. 2025. Available from: <https://www.ontario.ca/files/2025-03/moh-schedule-benefit-2025-03-19.pdf> Last accessed: January 12, 2026.
 26. Thusini S, Milenova M, Nahabedian N, Grey B, Soukup T, Chua KC, et al. The development of the concept of return-on-investment from large-scale quality improvement programmes in healthcare: an integrative systematic literature review. *BMC Health Serv Res.* 2022;22(1):1492.
 27. Bonnabry P, Francois O. Return on investment: a practical calculation tool to convince your institution. *Eur J Hosp Pharm.* 2020;27(2):111–3.
 28. Agency for Healthcare Research and Quality (AHRQ). Return on Investment Estimation. Toolkit for Using the AHRQ Quality Indicators. How To Improve Hospital Quality and Safety. Rockville, MD; 2013.

29. Wikipedia. Stock exchange [Available from: https://en.wikipedia.org/wiki/Stock_exchange%22_/o_%22Stock_exchange Last accessed: January 12, 2026.
30. Pechlivanoglou P, Abrahamyan L, MacKeigan L, Consiglio GP, Dolovich L, Li P, et al. Factors affecting the delivery of community pharmacist-led medication reviews: evidence from the MedsCheck annual service in Ontario. *BMC Health Serv Res.* 2016;16(1):666.
31. Gurwitz JH, Field TS, Harrold LR, Rothschild J, Debellis K, Seger AC, et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. *JAMA.* 2003;289(9):1107–16.
32. Roohi E, Lo C, Martinusen D, Levin A. Structure and Function of a Provincial Renal Pharmacy Program: Applying the Chronic Care Model to Address Equitable Access to Medication and Pharmacy Services. *Can J Kidney Health Dis.* 2023;10:20543581231177840.
33. MacCallum L, Consiglio G, MacKeigan L, Dolovich L. Uptake of Community Pharmacist-Delivered MedsCheck Diabetes Medication Review Service in Ontario between 2010 and 2014. *Can J Diabetes.* 2017;41(3):253–8.
34. St Peter WL, Wazny LD, Patel UD. New models of chronic kidney disease care including pharmacists: improving medication reconciliation and medication management. *Curr Opin Nephrol Hypertens.* 2013;22(6):656–62.
35. Betts KA, Song J, Faust E, Yang K, Du Y, Kong SX, et al. Medical costs for managing chronic kidney disease and related complications in patients with chronic kidney disease and type 2 diabetes. *Am J Manag Care.* 2021;27(20 Suppl):S369–74.
36. Villiet M, Laureau M, Perier D, Pinzani V, Giraud I, Lohan L, et al. Emergency Department Visits for Medication-Related Events With vs Without Pharmacist Intervention: The URGEIM Randomized Clinical Trial. *JAMA Intern Med.* 2025;185(6):669–78.
37. Weber C, Beaulieu M, Djurdjev O, Er L, Taylor P, Ignaszewski A, et al. Towards rational approaches of health care utilization in complex patients: an exploratory randomized trial comparing a novel combined clinic to multiple specialty clinics in patients with renal disease-cardiovascular disease-diabetes. *Nephrol Dial Transpl.* 2012;27(Suppl 3):iii104–10.
38. Vassalotti JA, DeVinney R, Lukasik S, McNaney S, Montgomery E, Voss C, et al. CKD quality improvement intervention with PCMH integration: health plan results. *Am J Manag Care.* 2019;25(11):e326–33.
39. Grundy Q, Quanbury A, Hart D, Chaudhry S, Tavangar F, Lexchin J, et al. Prevalence and nature of manufacturer-sponsored patient support programs for prescription drugs in Canada: a cross-sectional study. *CMAJ.* 2023;195(46):E1565–76.

Figures

$$\text{Return on Investment (ROI)} = \frac{\text{Gain(s) from iVRx}}{\text{Cost of iVRx}} \times 100$$

Figure 1

Return on Investment (ROI) formula