Pharmacist prescribing and care improves cardiovascular risk, but is it cost-effective? A cost-effectiveness analysis of the R_xEACH study

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The R_xEACH study is the largest randomized controlled trial conducted in a community pharmacy setting. We were interested in evaluating the economic impact of pharmacist case finding, prescribing and care for cardiovascular risk reduction in a Canadian setting.

L'étude R_xEACH est l'une des plus importantes études contrôlées à répartition aléatoire menées dans le milieu de la pharmacie communautaire. Nous voulions évaluer l'incidence économique de la recherche de cas, de la prescription et de la prestation de soins par les pharmaciens relativement à la réduction du risque cardiovasculaire dans un contexte canadien.

ABSTRACT

Background: The R_xEACH randomized trial demonstrated that community pharmacist prescribing and care reduced the risk for cardiovascular (CV) events by 21% compared to usual care.

Objective: To evaluate the economic impact of pharmacist prescribing and care for CV risk reduction in a Canadian setting.

Methods: A Markov cost-effectiveness model was developed to extrapolate potential differences in long-term CV outcomes, using different risk assessment equations. The mean change in CV risk for the 2 groups of R_xEACH was extrapolated over 30 years, with costs and health outcomes discounted at 1.5% per year. The model incorporated health outcomes, costs and quality of life to estimate overall cost-effectiveness. It was assumed that the intervention would be 50% effective after 10 years. Individual-level results were scaled up to population level based on published statistics (29.2% of Canadian adults are at high risk for CV events). Costs considered included direct medical costs as well as the costs associated with implementing the pharmacist intervention. Uncertainty was explored via probabilistic sensitivity analysis.

Results: It is estimated that the Canadian health care system would save more than $4.4 billion over 30 years if the pharmacist intervention were delivered to 15% of the eligible population. Pharmacist care would be associated with a gain of 576,689 quality-adjusted life years and avoid more than 8.9 million CV events. The intervention is economically dominant (i.e., it is both more effective and reduces costs when compared to usual care).

Conclusion: Across a range of 1-way and probabilistic sensitivity analyses of key parameters and assumptions, pharmacist prescribing and care are both more effective and cost-saving compared to usual care. Canadians need and deserve such care. *Can Pharm J (Ott)* 2019;152:257-266.

Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide, accounting for nearly one-third of the total deaths in 2016.[1] The majority of CVD cases can be prevented by addressing modifiable risk factors, which include tobacco use, hypertension, hyperlipidemia, diabetes, physical inactivity, high-fat diet and obesity.[1,2]

The major CVD risk factors are still substantially prevalent and undertreated, despite the risk associated with them and the advent of new treatments.[3-6] For example, Al Hamarneh[3] and colleagues found that almost 50% of community-dwelling Canadians with type 2 diabetes were not at their A1C target. Leiter and colleagues[4] reported that almost half of Canadians

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KNOWLEDGE INTO PRACTICE

- This is the first study to evaluate the cost-effectiveness of pharmacist case finding, prescribing and care in patients at high risk for cardiovascular disease in comparison to usual care in a community pharmacy setting.
- The Canadian health care system could save more than $4.4 billion over 30 years if the pharmacist intervention were delivered to only 15% of the eligible population.
- Pharmacist care would be associated with a gain of 576,689 quality-adjusted life years and avoid more than 8.9 million cardiovascular events.
- Such benefits, combined with the high level of evidence supporting pharmacist-led interventions in chronic diseases and the support and satisfaction of patients with those interventions, present policy makers and pharmacy associations with an opportunity to add 42,500 helping hands in Canada to tackle the largest health care problem in the world.

MISE EN PRATIQUE DES CONNAISSANCES

- Il s'agit de la première étude évaluant le rapport évaluant coût-efficacité de la recherche de cas, de la prescription et de la prestation de soins par les pharmaciens, par rapport à la prestation des soins habituels, dans le milieu de la pharmacie communautaire, chez des patients présentant un risque élevé de maladie cardiovasculaire.
- Le système de soins de santé canadien pourrait économiser plus de 4,4 milliards de dollars sur 30 ans si les pharmaciens intervenaient auprès de seulement 15 % de la population admissible.
- Les soins prodigués par les pharmaciens seraient associés à un gain de 576 689 années de vie ajustées en fonction de la qualité et permettraient d'éviter plus de 8,9 millions d'événements cardiovasculaires.
- Ces bienfaits, combinés aux données de grande qualité appuyant les interventions dirigées par les pharmaciens dans les cas de maladie chronique ainsi qu'au soutien et à la satisfaction des patients quant à ces interventions, permettent aux décideurs politiques et aux associations de pharmacies d'ajouter 42 500 ressources supplémentaires pour lutter contre le plus important trouble de santé au monde.

with type 2 diabetes did not achieve their A1C or cholesterol target, slightly more than one-third achieved their blood pressure targets and only 13% achieved the composite triple target. Such sobering facts combined with the societal and economic burden of CVD (yearly cost in Canada is around $21 billion divided between health care costs and loss of productivity)[7] highlight the need for new avenues to tackle CVD and its risk factors.

Pharmacists are frontline primary health care providers who see patients with, or at risk for, chronic diseases frequently.[8] As such, they are well positioned to systematically identify patients with or at risk for CVD and help manage their condition. The evidence for the efficacy of pharmacists' intervention in CVD and its risk factors has been well demonstrated in the literature.[9-13] The Alberta Vascular Risk Reduction Community Pharmacy Project (R_xEACH) was a large randomized controlled trial designed to evaluate the impact of pharmacist case finding, prescribing and care on cardiovascular (CV) risk in patients at high risk for CV events.[12] R_xEACH included patients with diabetes, chronic kidney disease (CKD), established vascular disease or primary prevention (Framingham risk >20%) who had at least 1 uncontrolled risk factor (i.e., blood pressure, low-density lipoprotein cholesterol, tobacco use or A1C).[12] The pharmacist intervention included patient assessment, laboratory assessment, individualized CV risk assessment and education about this risk, treatment recommendations, medication adaptation and prescribing, regular communication with the patient's family physician and regular follow-up every month for 3 months.[12] The study demonstrated a 21% reduction in risk for CV events compared to usual care.[12]

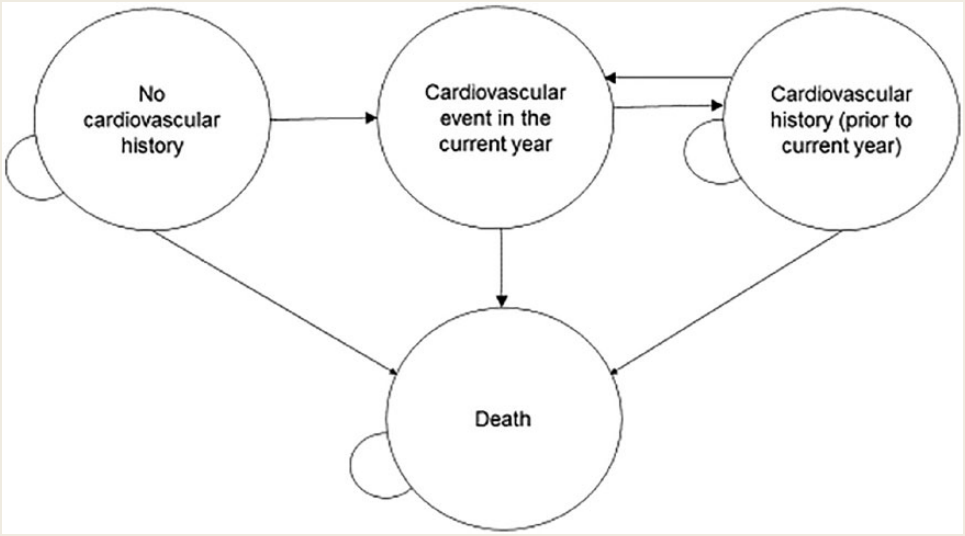
Despite the compelling evidence of the benefits of pharmacist management of CVD and its risk factors, there is scant evidence to support the economic value of providing such services as part of their routine care. As such, we conducted this analysis to evaluate the economic impact of pharmacist case finding, prescribing and care for CV risk reduction in a Canadian setting.

Methods

Model structure

The standard approach for pharmacoeconomic modelling in the absence of particular characteristics that might make an alternative approach is a Markov cohort cost-effectiveness model. As such, we developed a model (Figure 1), with health state characterized by cardiovascular history (none, within the current year, prior to the current year) (Table 1), from a third-party public payer perspective to extrapolate the reduction in long-term CV outcomes, resulting from

FIGURE 1 Markov model health states



pharmacist case finding, prescribing and care,[12] compared to a status quo scenario of usual care. The model was developed for a population with clinical characteristics as observed in the R_xEACH study population (mean age: 61.8 years), and the study's CV risk results were used to determine transitions between health states. The 10-year probabilities correspond to an annual transition probability for CV event of 3.1% for the usual-care group and 2.2% for the intervention group (that percentage will increase over time due to assumed waning of the intervention). The efficacy of the intervention assumed in the model was based on the 10-year CV risk scores calculated in the R_xEACH study for both treatment arms.[12] CV risk was calculated based on the patient's comorbidities (i.e., diabetes, CKD, previous vascular disease or primary prevention). The UK Prospective Diabetes Study (UKPDS) risk assessment equation[14] (see Appendix 1, available at www.cpjournal.ca, for risk factors included in the equation) was used to calculate CV risk in patients with diabetes. For primary prevention patients or those with CKD, CV risk was calculated using the Framingham risk assessment equation (Appendix 1).[15] In patients with previous vascular disease, the CV risk was calculated using the International Model to Predict Recurrent Cardiovascular Disease risk assessment equation (Appendix 1).[16] If the patient had more than 1 comorbidity, the risk was calculated using the relevant risk assessment equations, and the one estimating the highest risk was used. Risk over time was extrapolated from 10-year risk scores to a 30-year time horizon based on the assumption of exponential survival curves. Curves were calculated for both baseline and final risk scores for both treatment arms, and the difference in health and cost outcomes was compared across groups. For individuals who experienced a CV event, the distribution of specific event types (coronary heart disease, stroke, heart failure, myocardial infarction, angina) was based on Framingham calibration factors.[15]

A waning effect of treatment was incorporated, assuming that the intervention would be 50% effective after 10 years[17] and 0% effective after 30 years, with sensitivity analysis conducted based on 0% effectiveness after 15 and 20 years. Costs and outcomes were discounted at 1.5% per year.[18] Canadian life tables were used to calculate age- and sex-specific mortality over time. For individuals with a history of CVD, a hazard ratio of 1.71 was applied by multiplying with the relevant age- and sex-specific life table hazard (see Table 1).[19]

Individual-level results were scaled up to population level based on the assumption that 29.2% of Canadian adults[27] (approximately 9,000,000 people) would be eligible to receive the intervention (i.e., are at high CV risk). Of the full eligible population, it was assumed that only a subset would actually access the intervention, and results were calculated based on potential uptake rates of 15% of the eligible population, with sensitivity analyses conducted based on 30% and 45% uptake rates. In addition to the

TABLE 1 Markov model parameters and stochastic distribution for probabilistic sensitivity analysis

Parameter	Value	Probabilistic	Source
Base case			
10-year cardiovascular risk at baseline (pooled across treatment arms)	26.2%		R_xEACH study[12]
10-year cardiovascular risk at 3 months			
Usual care	26.3%	Normal (26.3, 1.05)	
Pharmacist intervention	20.2%	Normal (20.1, 0.86)	
Hazard ratio for mortality after cardiovascular disease	1.7	Lognormal (0.538, 0.075)	Pocock et al.[19]
Cost of pharmacist intervention*			Assumption
Year 1	$233.00		
Year 2	$175.00		
Year 3+	$175.00		
Cost of stroke†			Mittmann et al.,[20] Sorensen et al.[21]
Year 1	$82,323	Gamma (197.03, 417.83)	
Year 2+	$12,490	Gamma (25, 499.59)	
Cost per year of heart failure†	$13,637	Gamma (25, 545.50)	Bentkover et al.[22]
Cost per year of angina†	$3,877	Gamma (39.74, 97.56)	McGillion et al.[23]
Cost of myocardial infarction†			Coyle et al.[24]
Year 1	$11,857	Gamma (26.53, 446.93)	
Year 2+	$3468	Gamma (2.27, 1528.00)	
Cost of background medical costs	$6105		CIHI[25]
Utility			Sullivan et al.[26]
General population	0.867		
Post stroke	0.694	Beta (7090, 3126)	
Post heart failure	0.636	Beta (480, 275)	
Post angina	0.709	Beta (4843, 1988)	
Post myocardial infarction	0.725	Beta (61,446, 23,307)	
Disutility per year after age 70	0.00029		

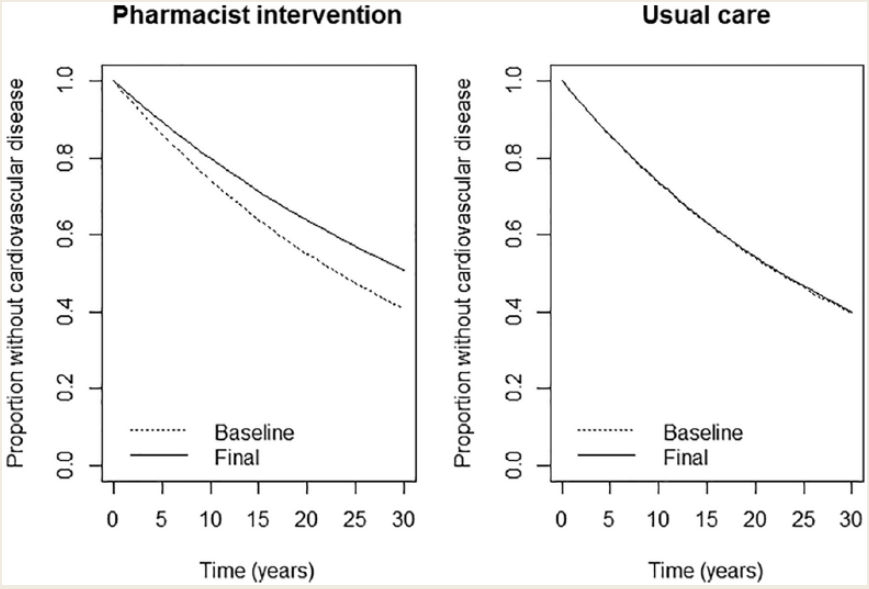
*The cost of pharmacist intervention for year 1 is composed of $125 (cost of baseline visit) + [3*$25] (cost of 3 follow-up visits) + [$500/15] (cost of half-day training [$500] distributed amongst 15 patients per pharmacist). The cost of pharmacist intervention from year 2 onwards is composed of $125 (cost of baseline visit) + [2*$25] (cost of 2 follow-up visits).

†Costs include all direct medical costs associated with the condition, including inpatient, outpatient, surgery and other procedures and medications.

prevalent population assumed to access the intervention initially, incident cases of high CV risk were also assumed to initiate the intervention each year. The same 15% uptake rate was assumed for incidence, and the incident rate was calculated based on the assumption that the ratio of incidence to prevalence would be the same for overall increased CV risk as has been reported for hypertension.[28,29]

Results were characterized by differences in costs, life years, quality-adjusted life years (QALYs) and incremental cost per QALY between treatment arms at both the individual and population levels. The distribution of results

FIGURE 2 Extrapolated risk of cardiovascular disease based on observed 10-year cardiovascular risk scores from R$_x$EACH study



was characterized by a 5000-iteration probabilistic sensitivity analysis. Model parameters were consistent with a recent model developed to assess the impact of pharmacist intervention on hypertension.[30]

Health state utility values

It has been reported that utility values are similar among patients in Canada and the United States.[31] As such, we used a published catalogue of EuroQol 5 dimension (EQ-5D) utility values to quantify health state utility values (HSUVs) for health states of interest. Resulting utilities were 0.725 (standard error [SE] 0.0015) for myocardial infarction (MI), 0.709 (SE 0.0055) for angina, 0.694 (SE 0.0046) for stroke and 0.636 (SE 0.0175) for heart failure. Resulting HSUVs were applied based on the occurrence of the first CV event; adjustments were not made for multiple events. A utility decrement of 0.00029 per year was applied to all years accrued older than age 70 years (e.g., for individuals surviving to age 75, a QALY decrement of $0.00029 \times 5 = 0.00145$).[26]

Costs

Costs included direct medical costs as well as the costs associated with implementing the pharmacist intervention. Investigators' familiarity with implementing such programs in a clinical trial setting provided the assumptions to calculate the cost of the pharmacist intervention (a similar approach was implemented in a recent model developed to assess the impact of pharmacist intervention on hypertension).[30] It was assumed that individuals would be seen 4 times in the first year and 3 times per year thereafter. The unit cost of the first consultation of each year is $125 CAD and $25 for subsequent consultations, reflecting the fee schedule in Alberta at the time the study was conducted.[32] Conservatively, we also assumed that there would be no difference in other background medical costs, despite the fact that the intervention group would likely have physician visits offset by the additional pharmacist consultations. All aspects of the intervention program are within the current core competencies of pharmacists in Alberta, and any additional training would likely be covered by the pharmacy or done as part of usual continuing professional development by pharmacists. However, as a conservative assumption, it was assumed that a government payer would contribute funding for a half-day training per pharmacist to familiarize themselves with the intervention and required documentation. Assuming $1000 per training-day to be distributed among 15 patients per pharmacist, the resulting cost is an additional $33 per patient receiving the intervention.

CVD costs were based on a review of the Canadian studies published in peer-reviewed journals. To inflate values to 2017 $CAD values,

we used the Canadian Health and Personal Care component of the Consumer Price Index.[33]

Based on Canadian Institutes for Health Information (CIHI) reports, $6105 per person per year was assumed to be the overall Canadian average background non-CV medical cost.[34] When building the base case, we used the overall average rather than age-specific values to prevent double-counting of costs. Since age-specific values in older individuals are expected to comprise a substantial proportion of CV-related costs, these are being explicitly incorporated into the model.

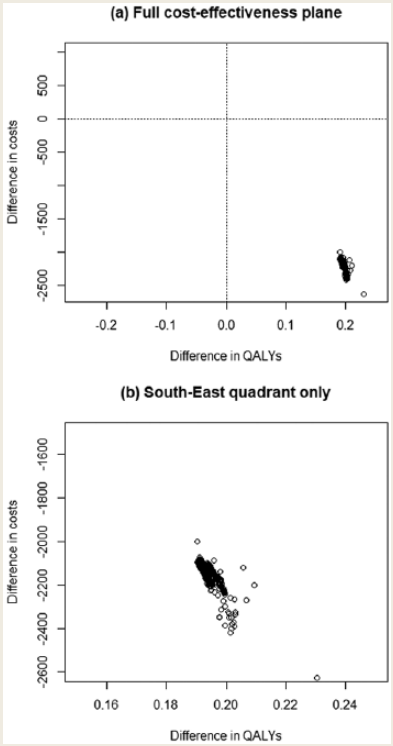
Results

In the R_xEACH study, the pooled baseline CV risk score for the entire study population was estimated to be 26.2%. At end of treatment, this risk score was reduced to 20.2% (SE 0.86%) in the intervention group and remained similar to baseline (26.3% [SE 1.05%]) in the usual-care group. Based on the assumption of an exponential function and extrapolating from 10-year risk scores, 30-year risk of CVD for both treatment arms is shown in Figure 2.

At the end of the 30-year time horizon, it is estimated that each individual accessing the pharmacist intervention would gain 0.11 life years and 0.19 QALYs, experience 0.10 fewer CV events, and accrue $2149 less in direct medical costs compared to an individual not receiving the intervention. For every 100 individuals accessing the intervention, it is estimated that the avoided CV events would include 3 cases of stroke, 5 MIs, 2 anginas and 1 heart failure. These differences result from reduced incidence of CV events predicted by the reduction in CV risk scores, leading to improved survival and lower medical costs. The intervention is therefore estimated to be economically dominant (i.e., more effective and less costly) relative to the usual care. The dominant result held in 100% of iterations of the probabilistic sensitivity analysis (5000 iterations) (Figure 3). (There is 100% probability of cost-effectiveness at all willingness-to-pay thresholds.) The overall dominant result remained when the maximum time at which the intervention waned to zero efficacy was reduced from the base case assumption of 30 years to 15 and 20 years.

When the individual-level results are scaled up to the population level, the base case assumption of a 15% uptake rate resulted in an estimated 1.3 million prevalent individuals accessing the intervention in the first year. It was assumed that

FIGURE 3 Cost-effectiveness plane across 5000-iteration probabilistic analysis



100,000 incident individuals would enter the cohort each year. For this population size, across probabilistic sensitivity analysis interventions, the mean incremental cost (discounted 1.5%) associated with the intervention was a savings of more than $4.4 billion over 30 years. Corresponding mean differences in health outcomes were an additional 576,689 QALYs, 380,143 life years, and more than 8.9 million fewer CV events. When uptake rates were increased to 30% or 45% of the eligible population, relative to the base case assumption of 15%, cost savings and health outcomes improvements increased accordingly (Table 2).

Discussion

To our knowledge, this is the first study to evaluate the cost-effectiveness of pharmacist case finding, prescribing and care in patients at high risk for CVD in comparison to usual care in a community pharmacy setting. Our results demonstrated that the pharmacist intervention was an economically dominant strategy compared to usual care, which means that the intervention both improves patient outcomes and saves the health care system money. Indeed, the

TABLE 2 Intervention impact on cost and outcomes over 30 years

	Proportion of eligible population accessing the intervention		
	15%	30%	45%
Incremental costs	–$4,403,946,776	–$8,807,893,551	–$13,211,840,327
QALYs	576,689	1,153,378	1,730,067
Life years	380,143	760,285	1,140,428
CV events avoided	8,915,842	17,831,684	26,747,527

CV, cardiovascular; QALY, quality-adjusted life year.

dominant result held in 100% of 5000 iterations of the probabilistic sensitivity analysis. Pharmacist care would save more than $4.4 billion, add 576,689 QALYs and prevent more than 8.9 million CV events over 30 years compared to usual care if applied to only 15% of the eligible adults in Canada. Those savings can reach more than $13 billion if the intervention is applied to 45% of the eligible Canadians.

Our findings are consistent with the findings of Marra and colleagues,[30] who evaluated the economic impact of a comprehensive community pharmacist intervention (including education and prescribing) in patients with uncontrolled hypertension. They reported that the intervention improved patient outcomes and was associated with cost savings compared to usual care. Similar cost reductions were found in our study.

Omboni and Caserini[35] and Altowaijri and colleagues[36] conducted systematic reviews to evaluate the clinical and economic effectiveness of pharmacist interventions in the management of CVD. They reported that such interventions (including medication management, patient education and direct measurement and management of CVD risk factors) were associated with reduced health care costs. This is consistent with our findings, in which each individual receiving the pharmacist intervention would accrue $2149 less in direct medical costs compared to an individual who is not.

Limitations

This study is not without limitations. The assumption required to extrapolate the observed data into long-term outcomes is an inherent limitation of any cost-effectiveness model. However, we conducted a series of extensive probabilistic and deterministic analyses as well as a series of threshold analyses to mitigate that limitation. The dominant result held in 100% of iterations of the probabilistic sensitivity analysis. For the base model, we have assumed that the intervention would be delivered to only 15% of the eligible population and used the Alberta fee schedule at the time of study conduct.[37] Such assumptions indicate that our model is very conservative. The difference in pharmacy fee schedule in other jurisdictions may affect the generalizability of the findings. However, our conservative assumptions and findings strongly suggest that such intervention could still be effective and cost-saving in any jurisdiction regardless of the fee schedule. Our study used the efficacy data from 1 study.[12] However, this study is the largest randomized controlled trial in a community pharmacy setting.[12]

The findings of this economic evaluation, the improved clinical outcomes in the R_xEACH study,[12] the high degree of support and appreciation for pharmacists' full scope of practice[38] and the fact that CVD is one of the leading causes of death in Canada[7] indicate the need to implement such effective and less costly interventions on a wide scale as a public health service.

The clinical,[12] qualitative[38] and economic findings of the R_xEACH study add to the body of evidence to support pharmacist-led interventions in chronic diseases. Pharmacists, pharmacy associations and payers should seize the opportunity and join the fight against the leading cause of death in the world.[1]

Conclusion

Across a range of 1-way and probabilistic sensitivity analyses of key parameters and assumptions, pharmacist case finding, prescribing and care are more effective and cost-saving compared to usual care. Such savings, combined with the high level of evidence supporting pharmacist-led interventions in chronic diseases[9-13] and the support and satisfaction of patients with those interventions,[38] present policy makers and pharmacy associations with an opportunity to add 42,500 helping hands[39] in Canada to tackle the largest health care problem in the world. ■

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Author Contributions: *Al Hamarneh, Johnston, Marra and Tsuyuki designed the study. Al Hamarneh and Johnston were involved in the data acquisition, analysis, interpretation and drafting the manuscript. Al Hamarneh, Johnston, Marra and Tsuyuki reviewed and approved the manuscript. All authors have made substantial contributions to the manuscript.*

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