RESEARCH PAPER

Costs and Benefits of Free Medications after Myocardial Infarction

Coûts et avantages de la médication gratuite après un infarctus du myocarde

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Abstract

Background: Although combination pharmacotherapy after myocardial infarction dramatically reduces morbidity and mortality, the full benefits of secondary prevention medications remain unrealized owing to medication non-adherence. Because financial barriers are a major determinant of non-adherence, we examined the costs and benefits of providing free medications to myocardial infarction patients who do not have private insurance and are ineligible for substantial public coverage.
Methods: An economic evaluation combining decision analysis and Markov modelling was conducted to compare full public coverage of secondary prevention medications with the status quo. Costs and benefits were estimated using Canadian data wherever possible. The main outcome was the incremental cost-effectiveness ratio measured in cost per quality-adjusted life-year (QALY) gained.
Results: From the perspective of the publicly funded healthcare system, full coverage resulted in greater quality-adjusted survival than the status quo (7.02 vs. 6.13 QALYs) but at increased cost ($20,423 vs. $17,173). The incremental cost-effectiveness ratio (ICER) for full coverage compared to the status quo was $3,663/QALY. This result was robust to a wide range of sensitivity analyses. In a secondary analysis from the perspective of government, the ICER for full coverage compared to the status quo was $12,350/QALY. In this analysis, the ICER was sensitive to changes in price elasticity, but remained below $50,000/QALY as long as the elasticity remained below –0.035.
Interpretation: Public payers in Canada should consider providing secondary prevention medications to myocardial infarction patients without private insurance free of charge. Full public coverage is cost-effective compared to the status quo.

Résumé

Contexte : Bien que la pharmacothérapie multiple suite à un infarctus du myocarde réduise sensiblement les taux de morbidité et de mortalité, on ne profite pas toujours des avantages de la médication secondaire préventive, en raison de la non adhésion au traitement. Étant donné que les obstacles financiers sont un des principaux déterminants de la non adhésion, nous avons examiné les coûts et les avantages liés à l'offre de médicaments gratuits aux patients qui ont subi un infarctus du myocarde, qui n'ont pas d'assurance privée et qui sont inadmissibles à une couverture publique suffisante.
Méthodologie : Une évaluation économique réunissant l'analyse décisionnelle au modèle de Markov a permis de comparer la couverture publique intégrale pour le traitement de prévention secondaire par rapport au statu quo. Les données canadiennes ont été employées pour estimer les coûts et les avantages, là où il était possible de le faire. Le principal résultat a trait au rapport coût efficacité différentiel mesuré selon le coût par années-personnes sans invalidité (APSI).
Résultats : Pour le système public de santé, la couverture intégrale se traduit par une

plus grande survie ajustée pour la qualité de vie comparé au statu quo (7,02 par rapport à 6,13 APSI), mais à un coût plus élevé (20 423 $ par rapport à 17 173 $). Comparé au statu quo, le rapport coût efficacité différentiel (RCED) pour la couverture intégrale est de 3663 $/APSI. Ce résultat demeure concluant en fonction des nombreuses analyses de sensibilité effectuées. Selon une analyse secondaire effectuée du point de vue du gouvernement, le RCED pour la couverture intégrale par rapport au statu quo indique un résultat de 12 350 $/APSI. Dans cette analyse, le RCED était sensible aux changements liés à l'élasticité-prix, mais demeurait sous la barre des 50 000 $/APSI si celle-ci avait une valeur plus faible que -0,035.
Interprétation : Au Canada, les contribuables devraient envisager l'offre gratuite de traitement de prévention secondaire aux patients qui ont subit un infarctus du myocarde et qui ne possèdent pas d'assurance privée. La couverture intégrale est économiquement rentable par rapport au statu quo.

Between 1980 and 2000, mortality from cardiovascular disease in Canada decreased by approximately 50%. A major contributor to this reduction in mortality has been the increased availability and usage of medications for secondary prevention after myocardial infarction (Ford et al. 2007). Clinical practice guidelines recommend that most myocardial infarction patients be prescribed a beta blocker, ASA, an ACE inhibitor and a statin indefinitely, and clopidogrel for one year (Smith et al. 2006). It has been estimated that the first four of these medications reduces mortality after myocardial infarction by 75% to 80% (Hippisley-Cox and Coupland 2005; Wald and Law 2003). The addition of clopidogrel for the first year after myocardial infarction further reduces the risk of cardiovascular death, reinfarction and stroke (Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators 2001; Chen et al. 2005). Nevertheless, despite advances in the prevention and treatment of myocardial infarction, cardiovascular disease remains responsible for over 30% of deaths in Canada (Statistics Canada 2007).

Many patients do not benefit from secondary prevention medications because of suboptimal adherence (Rasmussen et al. 2007). Although the reasons for poor adherence are varied, increasing evidence suggests that deductibles and co-payments are a major contributor (Goldman et al. 2007). Because the Canada Health Act covers only physician and hospital services, public coverage of pharmaceuticals in Canada is neither universal nor uniform. For example, seniors in Ontario pay only a nominal dispensing fee; an elderly couple in Manitoba with a combined annual income of $30,000 would be required to pay the full cost of an annual $1,100 medication bill; and a 55-year-old man living alone in Saskatchewan would be ineligible for any public drug coverage whatsoever (Demers et al. 2008). Although 58% of Canadians have private

drug insurance, co-payments in these plans can be substantial. Moreover, approximately 11% of Canadians have only catastrophic public coverage, and 4% have no coverage at all (Kapur and Basu 2005).

Given that lower patient charges are associated with improved adherence, and better adherence produces improved health outcomes, it is logical to consider providing effective medications to patients free of charge. Providing secondary prevention medications to myocardial infarction patients in the United States appears to be cost-effective and may even be cost-saving (Choudhry et al. 2007; Choudhry, Patrick et al. 2008). Our objective in this study was to examine the cost-effectiveness of providing free secondary prevention medications to myocardial infarction patients in Canada.

Methods

We performed a cost-utility analysis comparing two policy options, a full-coverage strategy and a status quo strategy. In the full-coverage strategy, the government would pay the full cost of five recommended medications (clopidogrel for one year, and a statin, beta blocker, ACE inhibitor and ASA indefinitely) to patients discharged alive after myocardial infarction. In the status quo strategy, the patient would pay the full medication cost out of pocket – the current situation for patients who do not have private pharmaceutical insurance and are ineligible for substantial public coverage.

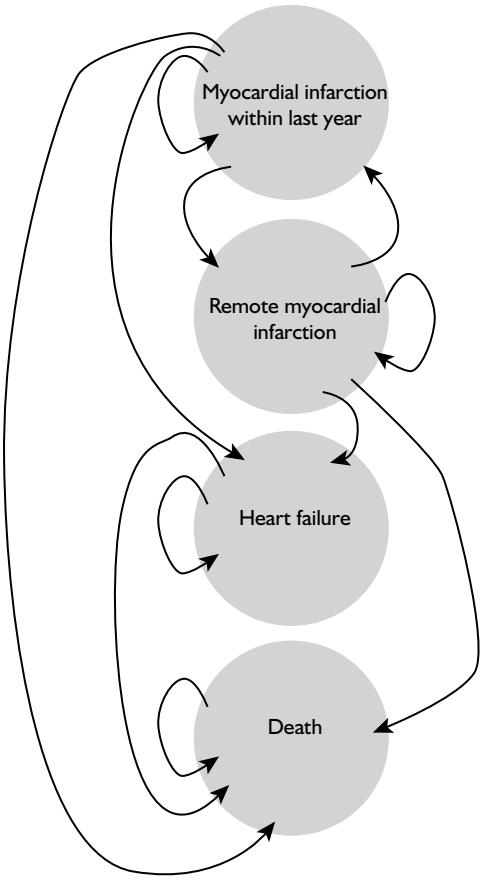
We followed guidelines for economic evaluation produced by the Canadian Agency for Drugs and Technologies in Health. We used a generic outcome measure, the quality-adjusted life-year (QALY), so that our results would be comparable across a variety of interventions and diseases. The QALY incorporates both quality and quantity of life and is the most widely used outcome measure in economic evaluations of health interventions. To be conservative, where assumptions were necessary we made them in a way that would favour the status quo. In addition to the description provided below, additional methodological details are provided in the Appendix to this paper.

Analytic model

We combined decision analysis with Markov modelling, simulating a cohort of patients discharged alive after myocardial infarction. In decision analysis, the expected benefits and cost of two or more options available to a decision-maker are formally compared by calculating the probability and utility of each of the various possible outcomes. Markov models are often used in economic evaluations of health interventions when an individual could transition between different health states in a stochastic manner. Our Markov model had four states: myocardial infarction within the last year, myocardial infarction more than one year ago, heart failure and death. Individuals

could transition through these states each year, as shown in Figure 1. A patient could be hospitalized once per cycle, and we ran the model for 50 years. The model was built following good practice guidelines (Briggs et al. 2006) and analyzed using the TreeAge Pro 2007 software package. As per Canadian guidelines, we used the perspective of the publicly funded healthcare system in our reference case. Medications paid for by patients are included as a cost in this analysis; costs due to lost productivity are not. Because of its relevance to public policy, we also considered the governmental perspective in a secondary analysis. In this analysis, medications paid for by patients are not included as a cost.

FIGURE 1. Model structure. Circles represent states and arrows represent possible transitions. A patient may be hospitalized, if alive, once during any cycle.



Model inputs

We used Canadian data for model inputs where possible and discounted costs and health outcomes at 5% per year in accordance with Canadian guidelines. Model inputs are summarized in Table 1; further details are provided in the Appendix.

TABLE 1. Model inputs

Parameter	Estimate for reference case	Range used for one-way sensitivity analysis	Source(s) for reference case estimate
Adherence			
Percentage of patients with optimal adherence under status quo	47.0%	30%–70%	Yan et al. 2007
Price elasticity	–0.16	–0.30 to –0.02	Contoyannis et al. 2005
Costs			
Cost of hospitalization	$9,363.45	50% to 200% of reference case estimate	Ontario Ministry of Health and Long-Term Care 2007; Bank of Canada 2008; Ontario Ministry of Health and Long-Term Care 2008b
Cost of medications in first year	$2,304.75		Ontario Ministry of Health and Long-Term Care 2008a
Cost of medications in subsequent years	$1,284.44		Ontario Ministry of Health and Long-Term Care 2008a
Percentage of drug costs incurred by optimally adherent patients	100%	—	N/A
Percentage of drug costs incurred by suboptimally adherent patients	0%	0%–100%	N/A
Percentage of drug costs paid by patient in full coverage strategy	0%	0%–100%	N/A
One-year event rates for untreated patients who have recently had a myocardial infarction			
Hospitalization	20.8%	50% to 200% of reference case estimate	Yan et al. 2004
Death	16.0%		Yan et al. 2004
Heart failure	13.3%		Tu et al. 2003
Reinfarction	13.6%		Tu et al. 2003
Risk reduction if treated	75%	40%–90%	Hippisley-Cox et al. 2005
One-year event rates for untreated patients who have heart failure			
Hospitalization	27.5%	50% to 200% of reference case estimate	Ko et al. 2008
Death	22.3%		Ko et al. 2008

TABLE 1. Continued

Risk reduction if treated	36%	20%–50%	Hippisley-Cox et al. 2005
Health state utilities			
Recent myocardial infarction	0.685	0.53–0.84	Clarke et al. 2002
Remote myocardial infarction	0.736	0.59–0.89	Clarke et al. 2002
Heart failure	0.663	0.51–0.81	Clarke et al. 2002
Death	0	—	N/A
Other parameters			
Ratio of events for patients in remote myocardial infarction state compared to recent myocardial infarction state	0.585	0.3–0.9	Capewell et al. 2000
Discount rate	5%	0-5%	Canadian Agency for Drugs and Technologies in Health 2006

ADHERENCE

We modelled adherence dichotomously, with patients being either optimally or suboptimally adherent (Choudhry et al. 2007). We estimated optimal adherence at 47.0% under the status quo strategy (Yan et al. 2007) and used a conservative estimate for demand price elasticity of –0.16 (Contoyannis et al. 2005), meaning that for every 1% increase in price there would be a 0.16% decrease in adherence. In the base case, optimally adherent patients were assumed to derive the full benefit of treatment and suboptimally adherent patients none of the benefit. In sensitivity analyses, we varied the relative benefit of combination pharmacotherapy extensively, recognizing that suboptimally adherent patients may in fact consume a significant proportion of their prescribed medications.

COSTS

We used recent guidelines to determine which medications should be taken by myocardial infarction patients (Smith et al. 2006). Within a drug class, we chose medications and dosages based on assumptions that are consistent with current practice – enteric-coated ASA 81 milligrams daily, metoprolol 50 milligrams twice daily, ramipril 10 milligrams daily and atorvastatin 80 milligrams daily indefinitely, and clopidogrel 75 milligrams daily for one year. We used the Ontario Drug Benefit formulary to obtain prescription drug costs (Ontario Ministry of Health and Long-Term Care 2008a) and visited a commonly used pharmacy chain to estimate the cost of ASA. For

the prescription medications, we also added pharmacy mark-up and dispensing fees consistent with legislation and current pharmacy practices.

We used 2006 data from the Ontario Case Costing Initiative (Ontario Ministry of Health and Long-Term Care 2007) to estimate the cost of a hospitalization for the most frequent complications that occur after myocardial infarction: heart failure, unstable angina and reinfarction. Because the variation in costs between these diagnoses was relatively small, we calculated a weighted average and used this as the estimate for all hospitalizations. We adjusted for inflation using the Canadian Consumer Price Index (Bank of Canada 2008). Because the data from the Ontario Case Costing Initiative do not include physician costs, we used the Ontario Health Insurance Plan fee schedule to estimate physician charges (Ontario Ministry of Health and Long-Term Care 2008b).

In accordance with Canadian guidelines, we did not include costs due to lost productivity or costs due to ongoing medical care. We also excluded time costs to patients and their families because these costs are difficult to estimate and overestimating them would have biased our study in favour of the full-coverage strategy.

OUTCOMES

Owing to the sequential introduction of secondary prevention medications into clinical practice, there are no randomized controlled trials comparing all five recommended medications with none. Accordingly, we used observational data to estimate relative risk and event rates. We estimated that combination pharmacotherapy would reduce adverse outcomes for individuals in the recent myocardial infarction or remote myocardial infarction states by 75%, using data from a published case-control analysis (Hippisley-Cox and Coupland 2005). We conservatively assumed that patients in the heart failure state would benefit only from beta blockers and ACE inhibitors and therefore estimated that treatment would reduce the risk of death by only 36% (Hippisley-Cox and Coupland 2005). This is likely a conservative assumption given that meta-analyses of beta blockers alone suggest a risk reduction of 38% (Fauchier et al. 2007). Because of the central importance of these parameters in our model, we varied them extensively in sensitivity analyses.

We used Canadian registry data and population-based observational studies to estimate the current rates of complications after myocardial infarction (Ko et al. 2008; Tu et al. 2003; Yan et al. 2004; Lee et al. 2004) and the proportion of patients currently receiving combination pharmacotherapy (Cox et al. 2005; Ko et al. 2008; Jackevicius et al. 2003).

Because complication rates are higher in the first year after a myocardial infarction than they are subsequently, we used long-term outcomes data from a population-based

study (Capewell et al. 2000) to estimate the ratio between outcomes after one year to outcomes in the first year. This ratio is consistent with estimates from long-term trial data (Law et al. 2002). Failing to make this estimation would have resulted in our model's inappropriately favouring the full-coverage strategy.

UTILITIES

We used EQ-5D survey data collected from patients enrolled in the United Kingdom Prospective Diabetes Study (UKPDS) to estimate health state utilities (Clarke et al. 2002). (The health state utility is a number corresponding to the desirability of a particular state of health. Perfect health has a value of one, and death has a value of zero.) Although most myocardial infarction patients do not have diabetes, we were unable to find a similarly relevant and rigorous study conducted in a non-diabetic population. The UKPDS study provided utility estimates for myocardial infarction within the previous year, myocardial infarction prior to the previous year, heart failure in the previous year and heart failure prior to the previous year. We averaged the two heart failure utility values to calculate the heart failure utility estimate for our model. According to convention, the utility of death was assumed to be zero.

> The results from our study suggest that providing free medications to myocardial infarction patients would result in significantly improved outcomes at relatively low cost …

Sensitivity analyses

In the reference case, we performed one-way sensitivity analysis on all parameters for which it was logical, as shown in Table 1. Because data to suggest upper and lower limits for each parameter are generally unavailable, and because probability sensitivity analysis was unfeasible owing to an absence of the necessary data required to estimate probability distributions, we chose very wide ranges to account for uncertainty associated with model inputs. We also altered the medication regimen in two clinically relevant ways: we substituted valsartan 160 milligrams twice daily (Pfeffer et al. 2003) for ramipril to consider patients who are intolerant of ACE inhibitors, and we extended the duration of treatment with clopidogrel indefinitely to consider patients with drug-eluting stents.

We performed a similar series of sensitivity analyses for the secondary analysis from the governmental perspective. In the secondary analysis we also varied the degree

of cost-sharing, because the degree of cost-sharing would be expected to have a significant impact on both adherence and government costs (further details in the Appendix).

Results

Reference case

The model predicted that implementing the full-coverage strategy would result in average survival of 7.02 QALYs after myocardial infarction at an average cost of $20,423 per patient. The status quo strategy resulted in average survival of 6.13 QALYs at an average cost of $17,173 per patient. The model predicted an average incremental improvement in health, with the full-coverage strategy of 0.89 QALYs at a cost of $3,250 per patient, for an incremental cost-effectiveness ratio (ICER) of $3,663/QALY (Table 2). The $314 difference in hospitalization costs between the two strategies was small compared to the $2,936 difference in medication costs. Before adjusting for quality of life, the model predicted an average increase in survival with the full-coverage strategy of 1.2 years.

TABLE 2. Costs and benefits in the reference case

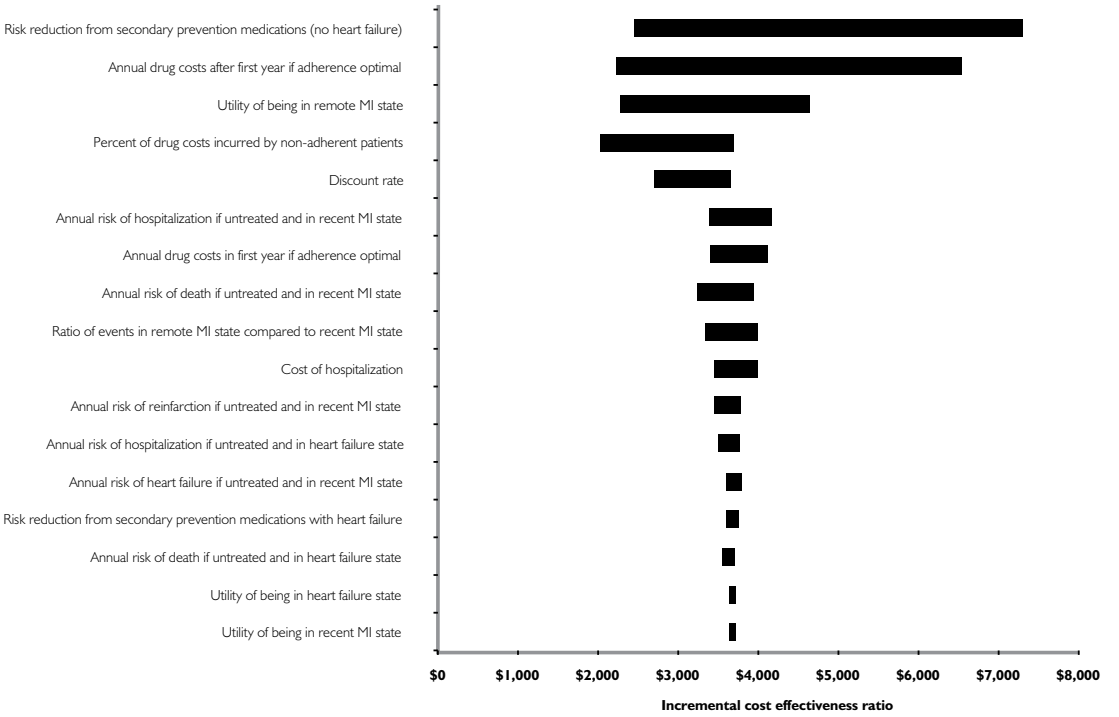
	Status quo	Full coverage	Difference
Costs ($)			
Prescription drugs	7,707	10,643	2,936
Hospitalizations	9,466	9,780	314
Total	17,173	20,423	3,250
Effectiveness (QALYs)	6.13	7.02	0.89
Incremental cost-effectiveness ratio ($/QALY)			3,663

Sensitivity analyses

The reference case results were robust to wide variations in all model inputs (Figure 2). The ICER was most sensitive to medication costs and the risk reduction conferred by combination pharmacotherapy. The model predicted that if medication costs after the first year could be lowered by 50%, the ICER would fall to $2,241/QALY, and that if the true risk reduction from secondary prevention medications were only 40%, the ICER would be $7,272/QALY.

Substituting valsartan for ramipril increased the ICER to $5,523/QALY, and extending the duration of treatment with clopidogrel indefinitely increased the ICER to $5,923/QALY.

FIGURE 2. Tornado plot showing one-way sensitivity analyses in the reference case



Analysis from a governmental perspective

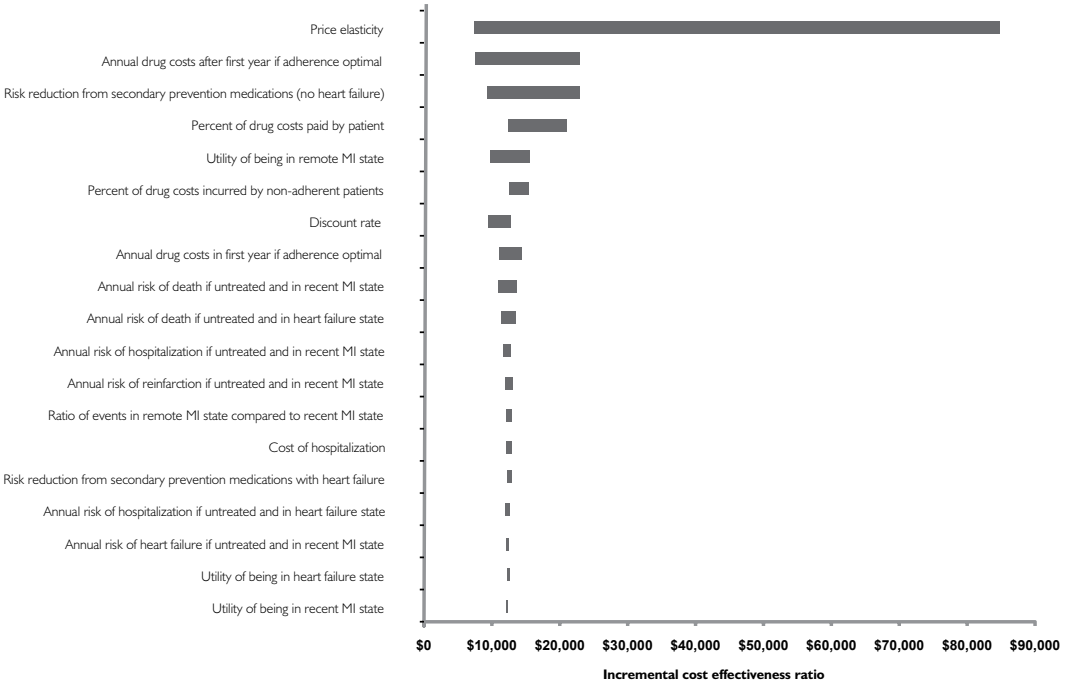
Because the governmental perspective model differed from the reference case only in its assignment of prescription drug costs, the average quality-adjusted survival in each arm and the cost in the full-coverage arm was the same as for the reference case. However, the cost in the status quo arm was much lower, as prescription drug costs in this arm are borne privately (Table 3). Comparing full coverage with the status quo, the model predicted an ICER of $12,350/QALY.

TABLE 3. Costs and benefits in the secondary analysis

	Status quo	Full coverage	Difference
Costs ($)			
Prescription drugs	0	10,643	10,643
Hospitalizations	9,466	9,780	314
Total	9,466	20,423	10,957
Effectiveness (QALYs)	6.13	7.02	0.89
Incremental cost-effectiveness ratio ($/QALY)			12,350

The results of the secondary analysis were most sensitive to changes in elasticity (Figure 3). A threshold analysis showed that the elasticity would have to approach perfect inelasticity (elasticity closer to zero than –0.035) for the ICER to exceed $50,000/QALY. Varying the degree of cost-sharing in the status quo arm had a relatively small effect.

FIGURE 3. Tornado plot showing one-way sensitivity analyses in the secondary analysis



Discussion

Complications after myocardial infarction are common and result in significant morbidity and mortality. Adherence to medications proven to reduce these complications is suboptimal, and a major reason for poor adherence is cost. The results from our study suggest that providing free medications to myocardial infarction patients would result in significantly improved outcomes at relatively low cost; the incremental cost-effectiveness ratios of $3,663/QALY from the perspective of the publicly funded healthcare system and the ICER of $12,350/QALY from the governmental perspective are both significantly below widely used thresholds used to decide whether novel health technologies should be eligible for public funding (Culyer et al. 2007; Laupacis et al. 1992).

Strengths and limitations

Our study has several strengths. First, we used population-based observational data for hospitalization costs, event rates and risk reductions. The findings from these studies are likely to be more representative of patients in clinical practice than data from randomized controlled trials (Avorn 2007). Second, despite conservative assumptions, our results were robust to very wide variations in model inputs. Finally, we discuss an intervention that is feasible and represents an innovative approach to improving health outcomes.

Several studies have examined the impact of cost-sharing on prescription drug adherence within government-funded pharmaceutical programs in Canada (Tamblyn et al. 2001; Li et al. 2007; Anis et al. 2005; Wang et al. 2008; Schneeweiss et al. 2007a,b), and at least one study has examined the impact of cost-sharing for patients who have private drug insurance (Ungar et al. 2008). Even with relatively small co-payments, all these studies have found that cost-sharing significantly reduces adherence even after myocardial infarction (Schneeweiss et al. 2007a,b). We are unaware of any Canadian studies comparing adherence between public drug plan beneficiaries and those without any drug coverage, but a study making this comparison in the American setting documented markedly reduced statin use among those without coverage (Federman et al. 2001).

Two studies have examined the cost-effectiveness of free medications after myocardial infarction in the United States, one in the context of a private insurance plan and one in the context of the government-funded Medicare program (Choudhry et al. 2007; Choudhry, Patrick et al. 2008). The US Medicare study found that free medications would likely be cost-saving from a societal perspective. In contrast, we found that free medications would result in health improvements but at increased cost – the typical circumstance associated with improvements in healthcare (Ginsburg 2004).

We may have underestimated the cost-effectiveness of providing secondary prevention medications for several reasons. First, we did not include stroke in our model because the available data were not as robust as for other outcomes, and we wished to be conservative rather than risk overestimating the cost-effectiveness of the full-coverage strategy. Medications used to reduce cardiovascular risk after myocardial infarction also reduce the risk of stroke (Fletcher et al. 2007), an outcome with both significant morbidity and cost. Second, we excluded outpatient costs, which would be higher for those who suffer post-MI complications. Third, we chose a medication regimen that is more expensive than that used in other studies (Choudhry et al. 2007; Choudhry, Patrick et al. 2008). Medication costs are also likely to decrease as patents expire, so the cost-effectiveness of full coverage would improve over time. Fourth, our risk reduction estimate may be overly conservative because it was calculated using data from patients who were treated before clopidogrel was used for secondary prevention.

Our study also has two noteworthy limitations. First, the dichotomization of

adherence in our model is an oversimplification. In clinical practice, patients may take anywhere from 0% to 100% of their recommended medication doses. However, simplification is obligatory in modelling, and one advantage of dichotomizing adherence is that it improves comprehension. To address this limitation we extensively varied the percentage of adherent patients, the drug costs of suboptimally adherent patients and the relative risk reductions in sensitivity analyses. Furthermore, in the analysis considering the governmental perspective, we performed a threshold analysis on elasticity, and determined that the elasticity would need to be very close to zero for the ICER to rise to $50,000/QALY. Second, we used data from the United Kingdom Prospective Diabetes Study to estimate health state utilities (Clarke et al. 2002) because similar data from a population of individuals without diabetes were unavailable. Because quality of life is reduced by the complications of diabetes more so than diabetes itself, we believe the usage of utilities from the UKPDS is reasonable. Moreover, because individuals with diabetes generally have worse health than individuals without diabetes, any potential bias introduced by using utilities from patients with diabetes would lead to our model's favouring the status quo strategy. This assertion is supported by the finding that health state utilities in the UKPDS study (Clarke et al. 2002) were lower than in a study of myocardial infarction patients (Tsevat et al. 1993).

Policy implications

The best evidence of the impact of providing free medications would come from a randomized controlled trial; such a trial is being undertaken within a private insurance plan in the United States, and results are expected in 2010 (Choudhry, Brennan et al. 2008). Whether a similar trial would be acceptable to policy makers in a publicly funded healthcare system like Canada's is uncertain (Maclure et al. 2007). Results from a trial conducted in a population of individuals with private insurance may also not be generalizable to Canadians with neither public nor private insurance. In the absence of trial data, policy makers may need to rely on modelling to assess the potential impact of new policies; these policies should then be rigorously evaluated as they are implemented.

The findings of our study suggest that policy makers should consider providing medications free of charge to myocardial infarction patients who do not have private insurance and are ineligible for substantial public coverage. Compared to drugs recently recommended for listing on provincial formularies in Canada, the full-coverage strategy described in our study has a highly favourable incremental cost-effectiveness ratio. For example, compared with standard care, adalimumab in Crohn's disease has an incremental cost-effectiveness ratio of over $100,000 per QALY (Canadian Agency for Drugs and Technologies in Health 2007).

Although it would likely be feasible from a technical standpoint to provide free medications only to patients who have suffered a myocardial infarction, it is unclear

whether this would be good policy. Policy makers may wish instead to consider providing medications free of charge to all patients with chronic illnesses where specific drug treatments are known to be both highly cost-effective and associated with poor adherence. Prospective natural experiments confirm that policies that affect out-of-pocket pharmaceutical expenditures also affect adherence (Chernew et al. 2008; Doshi et al. 2009). Furthermore, formal economic evaluations demonstrate that eliminating out-of-pocket payments would likely be a cost-effective use of resources not only for secondary prevention after myocardial infarction but also for the prevention of kidney and cardiovascular disease in patients with diabetes (Rosen et al. 2005). Examples of other diseases where medications are highly effective yet associated with poor adherence include asthma, epilepsy, heart failure, hypertension, hyperlipidemia and osteoporosis. Economic evaluations might also demonstrate the cost-effectiveness of providing medications free for patients with these and other conditions. Obviously, the budget impact of providing medications for free would vary considerably by province, given the different structure of existing provincial insurance plans and the varying rates of private insurance coverage.

Such a change in Canadian pharmaceutical policy would be broadly consistent with what is called "value-based insurance" in the United States (Chernew et al. 2007). Value-based insurance designs impose significant cost-sharing on "low value" interventions and little or no cost-sharing on "high value" interventions. Taking the principles of value-based insurance to their logical end would result in a system of financing similar to Canada's coverage of physician and hospital care, where cost-effective interventions are generally provided free of charge and cost-ineffective interventions are not covered at all (Dhalla and Kiran 2008). Although the financing of physician and hospital care in the United States and Canada differs substantially, pharmaceutical financing in the two countries is more similar than the casual observer might suspect. In both countries, private insurance is the predominant source of financing for prescription drugs, public funding covers some of the population, and many individuals have no coverage at all. Providing medications free of charge where they are likely to have the most value is one way for policy makers in both countries to allocate limited public resources more efficiently than is currently the case.

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Appendix

Decision tree

A schematic of the decision tree is shown in Figure A1. A more detailed view of the "good adherence" node in the full-coverage strategy is shown in Figure A2. The structural design of the other three nodes at the same level of the tree is identical.

FIGURE A1. Decision tree schematic used for the cost-utility analysis

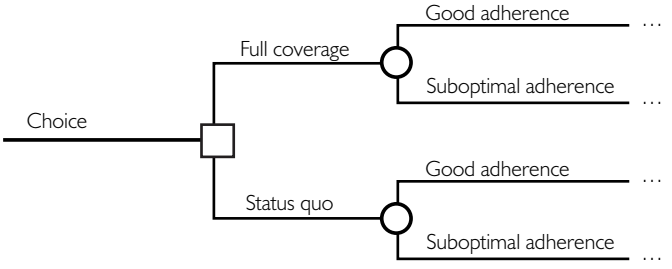
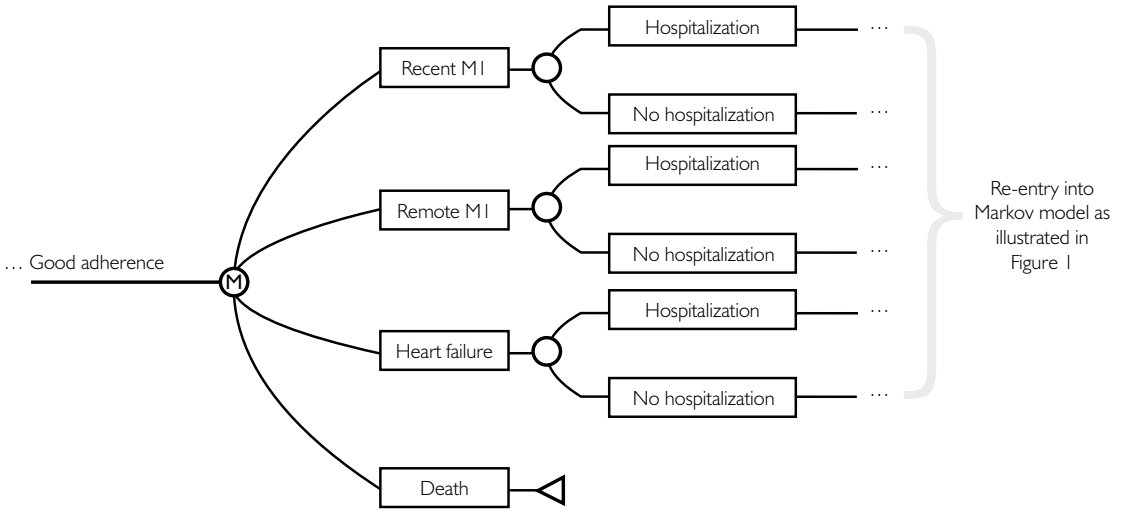


FIGURE A2. Schematic of the good adherence node



The square indicates the policy choice. Circles represent chance events, and the circle with "M" denotes entry into the Markov model.

Adherence and elasticity calculations – reference case

We used published data to estimate the rate of optimal adherence in the status quo arm and the price elasticity, and calculated the rate of optimal adherence in the full-coverage arm using the following formula:

$$e = (\Delta Q/Q_{avg})/(\Delta P/P_{avg})$$

where e represents elasticity, P represents price and Q represents quantity demanded. In the reference case we assumed that poorly adherent patients would pay for none of their drug costs and that optimally adherent patients would pay for 100% of their drug costs, giving $\Delta P/P_{avg} = 1/2$. This gives

$$e = (\text{adherence}_{SQ} - \text{adherence}_{FC})/(\text{adherence}_{FC} + \text{adherence}_{SQ})$$

where adherence_{SQ} and adherence_{FC} represent the proportion of adherent patients in the status quo and full-coverage arms, respectively. Solving for adherence_{FC} gives

$$\text{adherence}_{FC} = \text{adherence}_{SQ}*(1-e)/(1+e)$$

The reference case estimates of 47.0% for adherence_{SQ} and –0.16 for elasticity result in $\text{adherence}_{FC} = 64.9\%$.

Adherence and elasticity calculations – secondary case

In the secondary case, we allowed varying degrees of cost-sharing because of its impact on government costs. The same general formula is used, but because the price (to the patient) varies according to the degree of cost-sharing, the solution for adherence_{FC} is different. In this case

$$\text{adherence}_{FC} = \text{adherence}_{SQ}*(1-e_{CS})/(1+e_{CS})$$

where

$$e_{CS} = e*(1-f)/(1+f)$$

where f is the proportion of costs paid by the patient.

Event rates

We calculated event rates for adherent and non-adherent patients as follows: current event rate = (event rate in adherent patients x proportion receiving combination pharmacotherapy) + (event rate in non-adherent patients x proportion not receiving combination pharmacotherapy), with the event rate in adherent patients equal to the event rate in non-adherent patients multiplied by the relative risk (Choudhry, Patrick et al. 2008).

Estimation of ratio between events in remote myocardial infarction and recent myocardial infarction states

We used mortality data from Scotland (Capewell et al. 2000) to estimate the ratio between events in the remote myocardial infarction state and the recent myocardial infarction state. The Scotland data provided a 30-day survival rate, a one-year survival rate and a 10-year survival rate. We equated 30-day survival to discharge survival, and then used the one-year survival rate and the 30-day survival rate to calculate a one-year post-discharge mortality rate. In a similar fashion, we used the 10-year survival rate and the one-year survival rate to determine the proportion of patients who died between one and 10 years after study enrolment. We used this proportion to calculate an instantaneous event rate using the formula

$$\text{rate} = -[\ln (1 - \text{proportion})]/\text{time}$$

and then the formula

$$\text{one-year probability} = 1 - \exp(-\text{rate})$$

to calculate the annual death rate from years 2 to 9, as recommended in modelling texts (Briggs et al. 2006). We then compared this value to the one-year mortality rate to estimate the ratio of deaths in the remote myocardial infarction state compared to the recent myocardial infarction state. Finally, we assumed this ratio was the same for reinfarction and progression to heart failure as it was for death. Because of the uncertainty involved in estimating this ratio, because the ratio is non-constant in reality and because it is likely to be different for the different outcomes of interest, we varied this parameter extensively in a sensitivity analysis.