RESEARCH

Cost-effectiveness of self-managed versus physician-managed oral anticoagulation therapy

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Abstract

Background: Patient self-management of long-term oral anticoagulation therapy is an effective strategy in a number of clinical situations, but it is currently not a funded option in the Canadian health care system. We sought to compare the incremental cost and health benefits of self-management with those of physician management from the perspective of the Canadian health care payer over a 5-year period.

Methods: We developed a Bayesian Markov model comparing the costs and quality-adjusted life years (QALYs) accrued to patients receiving oral anticoagulation therapy through self-management or physician management for atrial fibrillation or for a mechanical heart valve. Five health states were defined: no events, minor hemorrhagic events, major hemorrhagic events, thrombotic events and death. Data from published literature were used for transition probabilities. Canadian 2003 costs were used, and utility estimates were obtained from various published sources.

Results: Self-management resulted in 3.50 fewer thrombotic events, 0.78 fewer major hemorrhagic events and 0.12 fewer deaths per 100 patients than physician management. The average discounted incremental cost of self-management over physician management was found to be $989 (95% confidence interval [CI] $310–$1655) per patient and the incremental QALYs gained was 0.07 (95% CI 0.06–0.08). The cost-effectiveness of self-management was $14 129 per QALY gained. There was a 95% chance that self-management would be cost-effective at a willingness to pay of $23 800 per QALY. Results were robust in probabilistic and deterministic sensitivity analyses.

Interpretation: This model suggests that self-management is a cost-effective strategy for those receiving long-term oral anticoagulation therapy for atrial fibrillation or for a mechanical heart valve.

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Long-term oral anticoagulation therapy with vitamin K antagonists is prescribed as prophylaxis against strokes and other embolic events in patients with atrial fibrillation or a mechanical heart valve.[1,2] Warfarin therapy, however, is complicated by the variability of its biologic effect, its narrow therapeutic index, and the associated thrombotic or hemorrhagic events in the event of over- or underanticoagulation.[2] It has been shown that improved anticoagulant control can be achieved through frequent monitoring of the international normalized ratio (INR), resulting in improved health outcomes.[3]

Monitoring the INR and managing warfarin dosing by a primary care physician is the current clinical standard of practice in Canada.[4] Physician management requires patients to visit a laboratory regularly for INR testing. The laboratory reports the INR to the physician, who subsequently contacts the patient with any required change in dosage. An alternative strategy is patient self-management. Self-management entails the measurement of the INR by the patient using a point-of-care device and, when necessary, self-adjustment of the warfarin dose using a nomogram.[4]

Several published trials have compared self-management with physician management or management in an anticoagulation clinic.[4–13] It has been found that patients who self-manage check their INR more frequently and are able to maintain a greater proportion of INRs within the therapeutic range compared with those whose therapy is monitored by a physician or in an anticoagulation clinic.[11–13] The results of a recent meta-analysis showed a significant reduction in thromboembolic events (odds ratio [OR] 0.45), major hemorrhagic events (OR 0.65) and all-cause mortality (OR 0.61) for those using a self-management or self-test strategy.[14] The results also showed that self-management compared with self-testing alone reduces the occurrence of thromboembolic events (OR 0.27) and death (OR 0.37).[14] These results, together with the greater initial costs of educating patients to self-manage and of the point-of-care device itself, provide the impetus for a formal cost-effectiveness analysis.

The objective of this study was to evaluate the incremental cost and health benefits of self-managed versus physician-managed chronic oral anticoagulation therapy from the perspective of the Canadian health care payer. A Bayesian approach was adopted to facilitate the incorporation of prior knowledge of transition probabilities and for probabilistic sensitivity analysis.

Methods

Model overview

We used a Markov decision-analytic model to compare the costs and quality-adjusted life years (QALYs) accrued to patients in a self-management or physician management strategy over a period of 5 years (online Appendix 1, available at www.cmaj.ca/cgi/content/full/1847/DC1). Patients could move through 5 health states: no events (state 1), minor or major hemorrhagic events (states 2 and 3), major thrombotic events (state 4) and death (state 5). Those who experienced a major hemorrhagic (state 3) or thrombotic event (state 4) were at risk of permanent disability and were switched to physician management if they were previously self-managing their therapy. The likelihood of patients changing from one health state to another depended on their time spent below, in and above therapeutic range.[15] Age-specific rates for natural death were derived from life tables from Statistics Canada.[16] At baseline, all patients were assumed to be in the "no events" state. The primary outcome was the incremental cost-effectiveness ratio (ICER), which has incremental costs in the numerator and incremental health benefits in the denominator. Cost and effects were discounted at a rate of 3% beyond the first year.[17]

The model was estimated using the Bayesian specialist software WinBUGS version 1.4.1 (MRC Biostatistics Unit, Cambridge, United Kingdom, 2004). To incorporate probabilistic sensitivity analysis, a Dirichlet distribution was specified to represent each transition probability.[18] Standard deviations for costs were generated using a triangular distribution by assuming an increase/decrease in cost by 25%.

Model inputs

Estimates for time in therapeutic range were taken from a randomized controlled trial conducted at Vancouver General Hospital (VGH) that evaluated self-management and physician management of warfarin therapy in 140 patients with atrial fibrillation, a mechanical heart valve or venous thromboembolism; 13 patients in the self-management group discontinued therapy immediately after randomization.[4] Optimal therapeutic ranges depended on the indication for treatment (INR 2.0–3.0 for atrial fibrillation, INR 2.0–3.0 for aortic mechanical heart valve, INR 2.5–3.5 for mitral mechanical heart valve). Patients in the self-management group were in therapeutic range a greater percentage of the time than those in the physician management group (71.8% v. 63.2% respectively; $p = 0.14$).

To determine the probability of an event given time in therapeutic range and to characterize prior knowledge of time in therapeutic range, we conducted a search on MEDLINE (Jan. 1990 to Jan. 2005) for studies of directly monitored self-management or physician management with long-term vitamin K antagonists, therapeutic ranges similar to those in the VGH trial, and event rates related to all levels of anticoagulation ranges. No studies met the inclusion criteria for providing prior knowledge of time in therapeutic range. Esti-

mates for event probabilities given time in therapeutic range were taken from a large prospective cohort study (ISCOAT) that followed 2745 consecutive patients with heart valve prostheses, atrial fibrillation or venous thromboembolism.[19] To provide prior information for event transition probabilities, a study by Cannegieter and colleagues[20] involving patients with a mechanical heart valve was used. The probability of permanent disability after a major event was assumed to be 0.30 for thrombotic events[21–23] and 0.10 for hemorrhagic events.[24]

Costs were taken from the perspective of the health care payer and were reported in 2003 Canadian dollars. The costs of self-management training were obtained from a VGH fully-allocated cost model. In the VGH trial,[4] one pharmacist conducted 2 training sessions lasting for a total of 5 hours. We assumed that 3 patients would attend each session, the number recommended by the International Self-Monitoring Association for Oral Anticoagulation.[25] To include the costs of "training the trainer," we assumed the pharmacist would need one full work day to develop sufficient training expertise.

INR testing for physician management included 14 laboratory tests per year.[11] Each test was followed by a telephone consult from the physician directly to the patient. For self-management, we assumed that patients conducted weekly

Table 1: Estimated model variables

Variable	Mean (95% confidence interval)
Time spent below, in or above therapeutic range	
Self-management	
Below	0.150 (0.144-0.156)
In	0.718 (0.710-0.725)
Above	0.133 (0.127-0.137)
Physician management	
Below	0.273 (0.266-0.280)
In	0.632 (0.624-0.639)
Above	0.095 (0.090-0.100)
Event rate by time below, in or above therapeutic range	
Thrombosis	
Below	0.120 (0.09-0.14)
In	0.012 (0.008-0.015)
Above	0.006 (0.003-0.008)
Major hemorrhage	
Below	0.004 (0.001-0.009)
In	0.005 (0.002-0.006)
Above	0.059 (0.05-0.07)
Minor hemorrhage	
Below	0.00
In	0.040 (0.034-0.045)
Above	0.110 (0.096-0.117)
Death	
Following major thrombotic event	0.210 (0.140-0.300)
Following major hemorrhagic event	0.140 (0.090-0.180)

INR tests and contacted a pharmacist after each test during the first month and once a month thereafter. Patients in the self-management strategy would require one physician visit per year, and those in the physician management strategy would have 3 physician visits annually.

Resource utilization for a major thrombotic event included an emergency visit, diagnostic tests (e.g., CT scan, electrocardiogram, carotid duplex, etc.) and treatment.[26] We assumed that 10% of patients would receive tissue plasminogen activator. Patients having a major thrombotic event were expected to stay in hospital an average of 15.3 days.[27] For major hemorrhagic events, cost data were based on a weighted average of costs for gastrointestinal bleed and intracranial hemorrhage.[28] The cost of a minor hemorrhage was limited to a complete blood count, an INR test and an emergency visit.

Our primary effectiveness end point was quality-adjusted life years (QALYs). QALYs are calculated by multiplying the duration of time spent in a health state by the utility weight for that state. In the base-case analysis, utility weightings associated with each health state were derived from several sources[29–31] that administered the EQ-5D questionnaire[32] to patients who experienced a major hemorrhage or stroke. In a deterministic sensitivity analysis, we examined the sensitivity of the ICER when standard gamble (SG) utility weightings[33] were used for the QALYs calculation.

An EQ-5D utility score of 0.70 was assigned to those patients after stroke with no permanent disability and was calculated as a weighted average of patients with a Barthel Index score of at least 15.[31] For those with permanent disability secondary to stroke, we assumed a utility weight of 0.19 for the first year, which was based on a weighted average of those having a Barthel Index score between 0 (very severe) and 14 (moderate).[31] In subsequent years, patients with disability from stroke were given a utility score of 0.33.[31] A utility weight of 0.80 was given to patients having a major hemorrhage with no disability.[30] For those with disability, an EQ-5D weight of 0.69 was assumed.[30]

Results

Estimates for the time in therapeutic range are presented in Table 1. In the self-management strategy, patients were estimated to spend 15% of time below, 72% within and 13% above therapeutic range. Those whose therapy was physician-managed were below range 27%, in range 63% and above range 10% of time. The probability of a thrombotic event if a patient was below, within or above therapeutic range was 0.12, 0.012 and 0.006 respectively. For major hemorrhagic events, the probability was 0.004, 0.005 and 0.059 for below, within and above therapeutic ranges. The probability of death given a thrombotic event was estimated to be 0.21. After a major hemorrhage, the probability of death was 0.14.

Start-up costs for self-managing patients were estimated to be $1567 per patient, and the annual costs of physician management and self-management were estimated to be $357 and $352 respectively per patient. The total acute cost for a major thrombotic event was $14 428. The estimated cost of a major and minor hemorrhage event was estimated to be $6003 and $91 respectively. After a major event, patients with mild disability underwent one year of rehabilitation at a cost of $2176.[34] For those with permanent disability, we estimated an average yearly cost of $33 532 for care.[35] Costs are summarized in online Appendix 2 (www.cmaj.ca/cgi/content/full/174 /13/1847/DC2).

Over a 5-year period, self-management was expected to result in 3.5 fewer major thrombotic events, 0.79 fewer major hemorrhagic events and 0.12 fewer deaths per 100 patients than physician management (Table 2). The mean cost per patient over 5 years in the self-management strategy was $6116 (95% confidence interval [CI] $5426–$6830). In the physician management strategy, the cost per patient was $5127 (95% CI $4390–$5894). As such, the average per-patient incremental cost of self-management when compared with physician management was $989 (95% CI $310–$1655). In terms of quality of life, self-management resulted in 4.28 QALYs (95% CI 4.24–4.30) and physician management in 4.21 QALYs (95% CI 4.19–4.25); the incremental QALY gained was 0.07 (95% CI 0.056–0.084) in favour of self-management. The incremental cost-effectiveness of self-managed long-term anticoagulation therapy over physician-managed was $14 129 per QALY gained over 5 years.

The decision to adopt a new strategy depends upon the maximum amount that decision-makers are willing to pay to achieve a benefit.[36] However, the maximum amount itself is unknown and must be varied to show how cost-effectiveness changes with willingness to pay. Fig. 1 illustrates the joint density of the incremental costs and benefits of each of the 20 000 model iterations; uncertainty surrounding the ICER

Table 2: Expected incremental costs and health benefits of self-managed anticoagulation therapy

Period	Events avoided per 100 patients			Mean cost,* $ (95% CI)	Mean Δ QALY† (95% CI)	ICER, $
	Major thrombotic	Major hemorrhagic	Death			
1 yr	0.72	0.17	0	1420 (1041 to 1807)	0.006 (0.005-0.008)	236 667
5 yr‡§	3.5	0.79	0.12	989 (310 to 1655)	0.07 (0.056-0.084)	14 129
10 yr§	5.67	1.25	4.1	599 (-459 to 1677)	0.20 (0.160-0.240)	2995

Note: CI = confidence interval, QALY = quality-adjusted life years, ICER = incremental cost-effectiveness ratio. All costs are reported in 2003 Canadian dollars.
*Incremental costs for self-management strategy.
†QALYs gained for self-management strategy.
‡Base case time period.
§Costs and QALYs were discounted at a rate of 3% beyond the first year.

can be summarized by considering the proportion of simulated ICERs below a given maximum amount per QALY, which is illustrated using the cost-effectiveness acceptability curve (Fig. 2).[36] In the base-case analysis, there was a 95% probability that self-management was cost-effective at a willingness to pay of $23 800.

Deterministic sensitivity analysis

We conducted 1-way and 2-way sensitivity analyses. Assuming no physician visits in either strategy produced an ICER of $19 514 over 5 years. Three visits in the self-management strategy and 6 visits in the physician management strategy resulted in an ICER of $11 428 per QALY gained. Decreasing the probability of disability from 0.30 to 0.25 after a major thrombotic event and from 0.10 to 0.05 after a major hemorrhagic event increased the ICER to $16 207 per QALY gained.
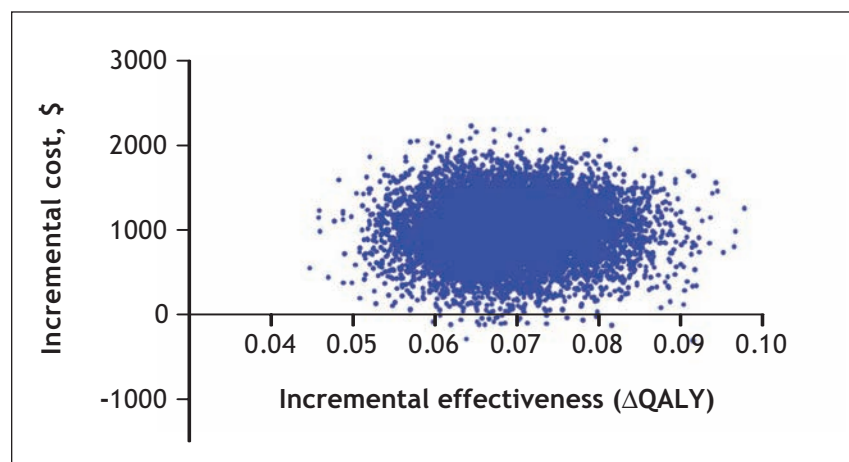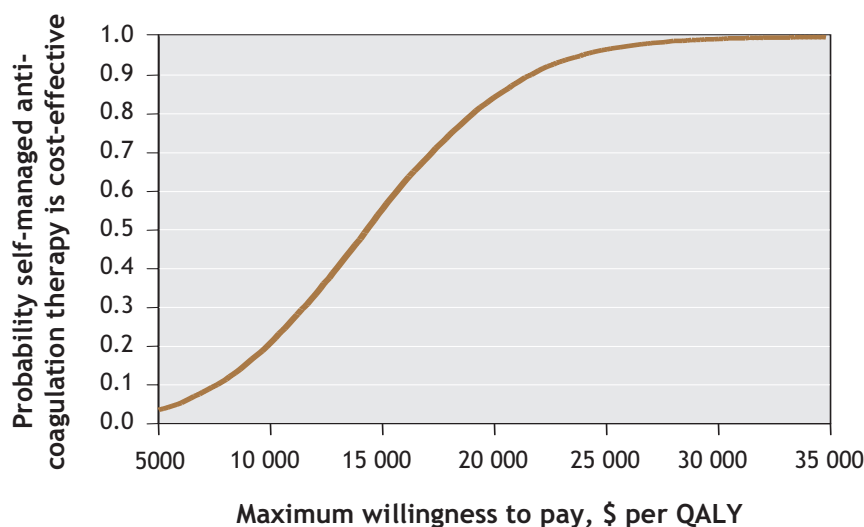
Increasing the discount rate to 6% produced an ICER of $15 712.

The sensitivity of the ICER to the assumptions surrounding utility weightings was tested by varying the starting utility of patients and using utility weights derived from the SG technique. Assuming that self-managed and physician-managed patients began with a utility weighting of 0.7 resulted in 0.063 QALYs gained and increased the ICER to $15 698. Hallan and associates[37] reported SG estimates of 0.91 and 0.61 for minor and major stroke. Using these as utility weightings for stroke resulted in an ICER of $18 314 per QALY gained. Thomson and associates[38] published SG utilities of 0.189 for a major stroke, 0.64 for a minor stroke and 0.84 for hemorrhage. These utility weightings gave an ICER of $14 544 per QALY gained.

A period of one year resulted in an ICER of $236 667 per QALY gained. Self-management becomes a more attractive option after 2 and 3 years with expected ICERs of $75 882 and $34 484 per QALY gained respectively. The cost-effectiveness of self-management over 10 years was $2995 per QALY benefit, assuming the point-of-care device would not have to be replaced.

Interpretation

Our analysis used a Bayesian framework to incorporate costs and QALYs into a fully probabilistic Markov model that examined self-managed oral anticoagulation therapy. The expected ICER was $14 129 per QALY gained over 5 years. Our model was robust to varying assumptions of resource utilization, the discount rate and quality of life. Although the threshold of what decision-makers are willing to pay for a QALY is a value judgment, in Canada it is generally accepted that a threshold of $50 000 per QALY represents good value given scarce health resources.[39] Therefore, over a 5-year period, our model suggests that self-management is a cost-effective option for a patient population taking warfarin for a mechanical heart valve or for atrial fibrillation.

Our study builds on previous economic evaluations in a number of important ways. Taborski and colleagues[40] reported that self-management was cost-saving over 10 years but did not consider differences in QALYs or adverse events forgone. Müller and colleagues[41] reported an ICER (Deutsche Marks [DM], year of currency not reported) of DM105 000 per life-year gained, but the main limitation to this study was using life-year gained as the primary outcome measure. Life-year gained will likely underestimate quality-of-life

Fig. 1: Joint density of the incremental costs and benefits of each of the 20 000 simulated cost-effectiveness ratios.

Fig. 2: Cost-effectiveness acceptability curve of maximum willingness to pay for self-managed anticoagulation therapy versus physician-managed anticoagulation therapy.

gains under a self-management strategy because differences in quality-of-life will be significant owing to avoidance of major disability. The US perspective on physician management versus management at an anticoagulation clinic, and anticoagulation clinic versus self-testing was explored by Lafata and colleagues;[42] this model used limiting assumptions for time in therapeutic range (i.e., 90% of time in therapeutic range for self-testing).

A limitation of our model is that it may not be applicable to all clinical populations with an indication for chronic anticoagulation therapy. This lack of generalizability is because the trial at the VGH[4] followed strict inclusion criteria. Inclusion criteria are necessary because the feasibility of self-management is dependent on the patient's ability to understand the concept of oral anticoagulant therapy and its potential risks as well as on adequate manual dexterity and sharpness of vision.[25] As such, although self-management appears to be economically attractive, it is unlikely that it will replace physician management for all patients.

A second limitation is that patient preferences for using the point-of-care device were not modelled. Although the ability of patients to successfully self-manage warfarin therapy is independent of age,[25] preferences for either management strategy may vary depending on age, confidence of participants, education level or comorbidity. We hypothesize it is these preferences that account for the high drop-out rate experienced (up to 20%) in previous self-management trials.[4,7] Subsequent economic analysis should stratify cost-effectiveness by indication and by preference for using the point-of-care device. This will aid in informing clinicians and decision-makers on which patients are most likely to benefit from self-management.

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