Selected reviews of economic evaluations relating to cardiology

A review of the cost of cardiovascular disease

Study Question: To review the literature on the economic costs of cardio-vascular disease (CVD) in Canada and other developed countries (United States, Europe and Australia) published from 1998 to 2006, with a focus on Canada.

Patient Group: Persons with cardio-vascular disease

Key Results: A total of 1656 titles and abstracts were screened, of which 34 articles were reviewed including six Canadian studies and 17 American studies. Seven studies estimated the costs associated with CVD, 10 for stroke, nine for hypertension two for congestive heart failure and nine for CAD. There was substantial variation between studies due to different methods of analysis, time horizon and countries or settings, though all studies concluded that the costs of treating CVD-related conditions are significant from both a payer and societal perspective. Several USA studies using administrative databases have shown that the cost associated with CVD conditions are higher than other chronic conditions. Around 82% of studies did not provide any information on the predictors of costs and multivariable regression analyses were conducted in 13% of studies to identify factors influencing cost figures. Just 28% of studies conducted sensitivity analyses and indirect costs were evaluated in 33% of studies.

Analysis of cost effectiveness of screening Danish men aged 65 for abdominal aortic aneurysm

Study Question: To assess the cost effectiveness of screening men aged 65 for abdominal aortic aneurysm via a screening programme is carried out by a team of mobile ultrasound technicians in a community setting. The comparator is no systematic screening. The study uses decision analytic modelling with a lifetime time horizon and adopts a healthcare perspective. A societal perspective is adopted in sensitivity analyses.

Patient Group: A hypothetical population of men aged 65 invited (or not invited) for ultrasound screening in the Danish healthcare system.

Key Results: Compared to no systematic screening, the estimated lifetime cost per QALY gained of screening is £43 485 (54 852 euros; US$71 160). The probability that screening is cost effective at a willingness to pay threshold of £30 000 is less than 30%. One way sensitivity analyses showed the incremental cost per QALY ratio varying from £32 640 to £66 001 per QALY. The authors conclude that screening for abdominal aortic aneurysm does not seem to be cost effective, and that further research is needed on long term quality of life outcomes and costs.
Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study

Study Question: To assess whether the mortality benefit from screening men aged 65-74 for abdominal aortic aneurysm decreases over time, and to estimate the long term cost effectiveness of screening. The study uses prospective data from a 4 centre randomised trial with a 10 year follow up.

Patient Group: 67,770 men aged 65-74 years, of whom 33,883 received an invitation to screening and 33,887 did not.

Key Results: Over 10 years the numbers of aneurysm related deaths in the invited and control groups were 155 and 296 respectively (relative risk reduction 48%, 95% confidence interval 37% to 57%). The degree of benefit accruing in earlier years of follow-up was maintained in later years. Compared to the control group the incremental cost per man invited for screening and the incremental cost per life year gained in the invited group were £100 (95% confidence interval £82 to £118) and £7600 (£5100 to £13 000) respectively. The incidence of ruptured abdominal aortic aneurysms in those originally screened as normal increased noticeably after eight years. The authors conclude that the UK national screening programme for abdominal aortic aneurysm should, in the long term, halve the mortality rate related to abdominal aortic aneurysm in men aged 65 or more, and that it will be a cost effective programme for the NHS. Rescreening of those originally screened as normal is not currently justified.

Relationship between adherence level to statins, clinical issues and healthcare costs in real-life clinical setting

Study Question: Statins have been shown to reduce the risk of major cardiovascular disease. We recognize that there is a major gap between the use of statins in actual practice and treatment guidelines for dyslipidemia. Low adherence to statins may have a significant impact on clinical issues and health-care costs. Therefore, the aim of this study was to evaluate the impact of low adherence to statins on clinical issues and direct health-care costs. In order to do this, a cohort of patients newly treated with statins was reconstructed from the Régie de l'Assurance Maladie du Québec and Med-Echo databases. The analysis was conducted from the perspective of the healthcare system.

Patient Group: Patients taking statins for the treatment of dyslipidemia. Data were taken from a cohort of 55,134 patients newly treated with statins who are on the Régie de l'Assurance Maladie du Québec and Med-Echo databases. There were a number of inclusion/exclusion criteria including subjects being aged between 45 and 85, initially free of cardiovascular disease, newly treated with statins between 1999 and 2002, and followed-up for a minimum of three years.

Key Results: The mean high adherence level to statins was around 96% during follow-up; and this value was at 42% for the low adherence level. The patients with low adherence to statins were more likely to have coronary artery disease (OR 1.07; 95% CI, 1.01-1.13), cerebrovascular disease (OR 1.13; 95% CI 1.03-1.25), and chronic heart failure within 3-year period of follow-up (OR 1.13; 95% CI 1.01-1.26). Low adherence to statins was also associated with an increased risk of hospitalisation by 4%
(OR 1.04; 95% CI 1.01-1.09). Among patients who were hospitalised, low adherence to statins was significantly associated with increase of hospitalisation costs by approximately $1,060/patient for a 3-year period. Based on these findings, the authors conclude that low adherence to statins was correlated with a higher risk of cardiovascular disease, hospitalisation rate, and hospitalisation costs. An increased level of adherence to statins agents should provide a better health status for individuals and a net economic gain.

**Fondaparinux versus enoxaparin in non–ST-elevation acute coronary syndromes: short-term cost and long-term cost-effectiveness using data from the Fifth Organization to Assess Strategies in Acute Ischemic Syndromes Investigators (OASIS-5) trial**


**Study Question:** Based on a randomized control trial (Fifth Organization to Assess Strategies in Acute Ischemic Syndromes Investigators [OASIS-5]) the aim of the study was to compare the short-term costs and long-term cost-effectiveness of 2 antithrombotics, fondaparinux (2.5 mg daily) and enoxaparin (1 mg per kg twice daily), for non–ST-elevation acute coronary syndrome. Treatment was administered for a mean of 5 days. The rationale of the study was that in OASIS-5 trial, fondaparinux patients were found to have about half the rate of major bleeding 9 days after randomization and at least as good clinical outcomes (death, myocardial infarction, major bleeding and stroke) after 6 months of follow-up. To undertake the economic evaluation, health care resource use and clinical efficacy data from the trial were incorporated into a cost-effectiveness model as applied to both for the time horizon of the trial (6 months) and over the longer term (life time). A societal perspective was adopted and the setting of the study was secondary care in the United States.

**Patient Group:** The patient group comprised of 20,078 male and female patients with non–ST-elevation acute coronary syndrome. Patients participated in the Fifth Organization to Assess Strategies in Acute Ischemic Syndromes Investigators [OASIS-5] trial. The economic analysis was based on a sub-sample of 759 trial patients.

**Key Results:** The effectiveness results showed that for each type of event over the 180-day follow-up period, fondaparinux is protective compared with enoxaparin, although this is not significant with nonfatal MI. For death, nonfatal MI and nonfatal stroke, increasing age, being male, a history of heart failure, and diabetes increase the event risk. ST depression and high creatinine at baseline increase mortality risk. Increased serum creatinine was the only predictive covariate for bleeds. The 180-day cost analysis indicated that fondaparinux would generate a cost saving of US$547 per patient (95% CI US$207-US$924). Sensitivity analysis suggested that savings could vary between US$494 and US$733. As well as mean (expected) cost-effectiveness, the probability of each therapy being the least costly and the more cost-effective assuming a cost-effectiveness threshold of US$50,000 per QALY gained was presented using probabilistic sensitivity analysis. Fondaparinux was predicted to generate a $188 saving and 0.04 additional QALYs in the “average” OASIS-5 patient. However, when 180-day cost and clinical results were extrapolated to long-term cost-effectiveness, fondaparinux was dominant (less costly and more effective in terms of quality-adjusted life-years) under most scenarios. The authors concluded that fondaparinux is a more cost-effective antithrombotic agent than enoxaparin in non–ST-elevation acute coronary syndrome. This is true
Cost-utility analysis of antihypertensive combination therapy in Japan by a Monte Carlo simulation model
Saito I, Kobayashi M, Matsushita Y, Mori A, Kawasugi K, Saruta T; Hypertension Research 2008; 31:1373-1383

Study Question: In this study, a pharmacoeconomic analysis of combination therapy including an angiotensin II receptor blocker (ARB) with other antihypertensive drugs was conducted based on the rationale that such combinations are widely used in daily clinical practice. A Markov model was constructed to analyze the prognosis of patients with essential hypertension and evaluate the cost-effectiveness of single-drug regimens with different ARBs and compared the cost-effectiveness of the first line drugs with that of combination therapy in cases in which additional antihypertensive drugs were added because the first-line drugs were not sufficiently effective. The cost-effectiveness of three therapeutic regimens - ARB monotherapy, calcium channel blocker (CCB) monotherapy and combination therapy with an ARB plus CCB (ARB + CCB) - in the presence or absence of diabetes in male and female patients. In the analysis, prognosis of hypertensive patients was analyzed by a Monte Carlo simulation model that can repetitively simulate the prognosis of individual patients. The analysis was conducted from the perspective of the payer, and direct medical and long-term care costs incurred after stroke were included in the expense items.

Patient Group: 55-year-old male and female hypertensive patients with a baseline systolic blood pressure (SBP) of 160 mmHg in the absence and presence of comorbid diabetes.

Key Results: In male hypertensive patients without diabetes, expected quality adjusted life years (QALYs) and cost per patient were 16.30 QALYs and Yen 6.21 million in the angiotensin II receptor blocker (ARB) group, 16.16 QALYs and Yen 6.07 million in the calcium channel blocker (CCB) group, and 16.70 QALYs and Yen 5.98 million in the ARB + CCB group. The QALYs were greater in the ARB + CCB group, followed by the ARB group and CCB group. The cost was lowest in the ARB + CCB group, followed by the CCB group and ARB group. Thus ARB + CCB was considered to be the dominant (less costly and more effective than comparator) therapy. In male patients with diabetes, QALYs and cost per patient in the ARB, CCB, and ARB + CCB groups were 14.69 QALYs and Yen 9.87 million, 14.25 QALYs and Yen 11.01 million and 15.15 QALYs and Yen 9.58 million, respectively. The QALYs were greatest in the ARB + CCB group, followed by the ARB group and CCB group. The cost was lowest in the ARB + CCB group, followed by the CCB group and ARB group. Thus ARB + CCB was considered to be the dominant therapy. In female patients without diabetes, expected QALYs were the greatest in the ARB + CCB group, followed by the ARB group and CCB group. The cost was lowest in the ARB + CCB group, followed by the ARB group and CCB group. Thus, ARB + CCB was considered to be the dominant therapy. In female patients with diabetes, the QALYs were greatest in the ARB + CCB group, followed by the ARB group and the CCB group. The cost was lowest in the ARB + CCB group, followed by the ARB group and CCB group. These results were similar to those obtained in male patients with diabetes. Thus, ARB + CCB was considered to be the dominant therapy and as a result, the incremental cost effectiveness ratio (ICER) assessment was not needed in all base-case analyses. The ARB + CCB group was the most cost-effective both in male and female patients with or without diabetes. The authors concluded that ARB + CCB combination therapy may be a more cost-effective lifetime antihypertensive strategy than monotherapy with either agent alone.
Cost-effectiveness of intensive atorvastatin treatment in high-risk patients compared with usual care in a postgeneric statin market: economic analysis of the aggressive lipid-lowering initiation abates new cardiac events (ALLIANCE) study
Mullins C D, Rattinger G B, Kuznik A, Koren M J; Clinical Therapeutics 2008; 30(2):2204-2216

Study Question: An economic model was developed to estimate the costs and benefits of intensive atorvastatin treatment in high-risk patients compared with usual care in a postgeneric statin market. The primary data source was the Aggressive Lipid-Lowering Initiation Abates New Cardiac Events (ALLIANCE) study, using the managed-care decision-maker’s perspective. This was a randomized, controlled, open-label, multicenter clinical trial that compared cardiovascular clinical outcomes in a total of 2,442 patients with established coronary heart disease. The primary outcome measure was clinical endpoints avoided. Direct medical costs included both the cost of care for each cardiovascular endpoint occurrence for an individual patient and medication costs for lipid-lowering therapy for all patients. The base-case model incorporated cardiovascular event rate data over a maximum of seven years of follow-up, with a mean of 51.5 months, as occurred in the trial. The base-case model assumed a three percent annual discount rate across the years and a US$ 10 difference in patient monthly prescription copayments between the treatment arms.

Patient Group: High-risk individuals with established coronary heart disease selected in the Aggressive Lipid-Lowering Initiation Abates New Cardiac Events (ALLIANCE) study were considered in this cost-effectiveness analysis.

Key Results: Study findings suggest that patients with established coronary heart disease constitute a population in which branded atorvastatin provides good economic value, even when compared with generic statins. The base-case model predicted higher pharmacy costs and greater medical offsets associated with atorvastatin. The increase in pharmacy costs to an insurer over the seven-year time horizon was US$3,881 per patient, whereas the reduction in direct medical costs over that same seven-year time horizon was US$2,860 per patient. The net increase to an insurer was US$1,021 per patient over seven years to achieve the net reduction in cardiovascular disease events. An incremental cost-effectiveness ratio (ICER) of US$10,344 was calculated for the base case, a seven year cost per clinical endpoint avoided model incorporating the Aggressive Lipid-Lowering Initiation Abates New Cardiac Events (ALLIANCE) study’s clinical events and drug costs. Scenario analysis exploring 3- and 5-year time horizons, monthly prescriptions co-payment differentials, and the impact of a generic atorvastatin suggest a range of ICERs from US$27,424 (in 2007) to a dominant strategy, whereby atorvastatin would be more effective and less costly.

Remote monitoring of implantable Cardioverter defibrillator patients: a safe, time-saving, and cost-effective means for follow-up

Study Question: The primary objective of the study was to evaluate whether an internet-based remote-monitoring service offers a safe alternative to office visits in implantable cardioverter defibrillator (ICD) follow-up. The secondary objectives were to assess: (i) the ease of use, satisfaction and acceptance of data interrogation and transmission by the patients, (ii) the ease of use and satisfaction of the clinicians with respect to reviewing device data via the website and (iii) the travel
burden on the patients and the workload of the clinic in order to calculate the economic impact of remote ICD monitoring.

**Patient Group:** Forty-one patients (34 (83%) males and 7 (17%) females) with a previously implanted implantable cardioverter defibrillator (ICD) supported by the Medtronic CareLink remote-monitoring service were included in the study. The mean age of the patients was 62 +/- 19 years (range 41-76 years). The indication for the ICD implantation was secondary prevention of sudden cardiac death in 37 (90%) patients and primary prevention in 4 (10%) patients. Thirty patients (73%) had prior myocardial infarction and 5 (12%) had dilated cardiomyopathy. Most of the patients were in stable clinical condition as only one patient (2%) had New York Heart Association III symptoms and no patients were in class IV (Table 1). The most common symptoms at study inclusion included occasional dyspnoea (32%) and palpitations (34%).

**Key Results:** During the study period, two generally recommended in-office visits were substituted by remote data transmission. A routine implantable cardioverter defibrillator (ICD) follow-up, including clinical and device evaluation by a cardiologist, at Oulu University Hospital costs €210. The fee to the municipality was €55 per transmission evaluation (i.e. the same as for a paper consultation). Thus, replacement of an in-office visit by a remote data transmission reduced the direct costs of ICD follow-up to the healthcare providers by €155. In addition, the patients saved €22 because they did not have to pay the fee for an outpatient visit. Accordingly, compared with the generally recommended ICD follow-up scheme, remote monitoring reduced the direct cost ICD follow-up among the study population from €38 048E to €23 534 (38%). The average travelling cost of the patients and the accompanying persons was €74.36 +/- €103.88 (range €1.20-€797.80) per outpatient visit. In contrast, no travelling expenses were caused by remote data transmissions. One patient had to make an overnight stop when visiting the device clinic and the total cost of accommodation among the study population was €20.18. In nine instances the patient (11%) and in 10 instances an accompanying person (12.5%) had to be on sick-leave because of the routine in-office visits. By using the average value of daily sickness allowance (€44.00 per day), it was calculated that the cost for the sickness allowance during the study period was €836E. No subjects were on sick leave due to remote monitoring. Eliminating the need for travelling and sickness allowance during remote monitoring reduced the indirect cost of ICD follow-up by €6954. There were 18 unscheduled patient- or physician-initiated data transmissions during the study period. In all of these cases, the physicians were able to address the problems remotely and there was no need for additional travelling and daily sickness allowance. The authors concluded that the launch of remote monitoring is an important milestone in the management of ICD patients. It provides a tremendous convenience for patients and clinicians and reduces the cost of follow-up. Although the technology is not intended to replace direct patient contacts completely, it can indeed release resources for other activities and help to maintain proactive patient care.