

# Economic impact of reduced incidence of diabetes in patients with left ventricular dysfunction treated with enalapril

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Presented at the 2005 Canadian Association for Population Therapeutics Conference, Vancouver, BC, April 17-19, 2005

## ABSTRACT

**Background:** In a subgroup of patients participating in the Studies of Left Ventricular Dysfunction (SoLVD) trials, the angiotensin-converting enzyme inhibitor enalapril was found to reduce incidence of new-onset diabetes by 78% relative to standard care alone. This study estimates the economic consequences of this reduced incidence of diabetes in patients with heart failure who receive enalapril, from a Canadian Ministry of Health perspective.

**Methods:** A 10-year Markov decision model was generated, incorporating published incidence data from the SoLVD trials and Canadian direct costs. The timeframe of the model reflects the life expectancy of patients in the SoLVD prevention trial.

**Results:** On average over 10 years, patients treated with enalapril incurred Can\$13,015 per person in treatment costs relating to diabetes and heart failure; those who did not receive enalapril incurred costs amounting to Can\$16,952. Enalapril was predicted to save \$3,938 per patient in diabetes and heart failure treatment costs over 10 years. Of patients surviving at model termination, 45.4% of those who did not receive enalapril and 82.4% of those who received enalapril were non-diabetic. These results were fairly robust to changes in the model assumptions.

**Conclusions:** Use of enalapril in patients with heart failure was projected to reduce treatment costs over 10 years as a consequence of reduced incidence of diabetes. When the benefits of reduced new onset of diabetes are added to the previously established benefits of enalapril resulting from reduced cardiovascular events, enalapril therapy in patients with heart failure becomes even more clinically and economically attractive.

## INTRODUCTION

- About 1% of Canadians aged 12 and over have heart failure (HF)<sup>1</sup>
- Diabetes mellitus increases risk of all-cause mortality and HF hospitalization in patients with left ventricular dysfunction<sup>2,3</sup>
- People with diabetes are at increased risk for cardiovascular disease, nephropathy, retinopathy and neuropathy
- Angiotensin-converting enzyme inhibitors (ACEIs) reduce morbidity and mortality in HF patients<sup>4</sup> and reduce risk of cardiovascular events and slow deterioration of renal function in diabetes patients<sup>5-8</sup>
- Analysis of 291 Canadian patients who participated in the Studies of Left Ventricular Dysfunction (SoLVD) found that the ACEI enalapril reduced incidence of new-onset diabetes relative to standard care plus placebo (5.9% vs 22.4%, P<.0001; hazard ratio 0.22, 95% confidence interval 0.10-0.46; mean follow-up 2.9 years).<sup>9</sup>

## OBJECTIVE

- This study models the economic impact of reduced incidence of diabetes in HF patients treated with enalapril from a Canadian health care system perspective

## METHODS

### Model

- Markov decision model with 1-year cycle length and 5- or 10-year time horizon (TreeAge Pro 2004, TreeAge Software, Williamstown, MA)
- Standard care vs standard care plus enalapril
- Three health states: diabetes-free, diabetes, death (see Figure 1)
- Probabilities of changing state were calculated<sup>10</sup> based on published data (see Table 1)
- Years of life were not discounted

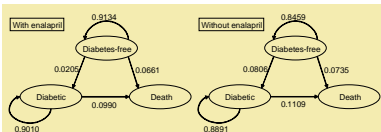


Figure 1. State transition models for patients receiving or not receiving enalapril. Numbers indicate the annual probabilities for the various state transitions.

Table 1. Annual probabilities, base case

Parameter	With enalapril	Without enalapril	Source
Probability of death in non-diabetic patients with HF	0.0661	0.0735	3
Probability of death in diabetic patients with HF	0.0990	0.1109	3
Probability of becoming diabetic	0.0205	0.0806	9

### Costs

- All costs are in 2004 Canadian dollars and were discounted 3% annually
- Costs of treating diabetes (including all complications) and HF were obtained from published Canadian studies (see Table 2)
- To avoid double-counting HF costs in patients with diabetes and HF, the cost of diabetes treatment was reduced by the proportion of patients with diabetes who have HF (see Table 2)
- No costs were assigned for transition from one state to another
- Enalapril cost was not included because it is used to treat HF and not to prevent diabetes

Table 2. Cost parameters, base case

Parameter	Value	Source(s)
(a) Annual HF treatment cost (Can\$)	1727	11
(b) Annual diabetes treatment cost, including all complications (Can\$)	4146	12
(c) Proportion of diabetic patients with HF	0.024	1, 13
(d) Annual diabetes treatment cost, excluding HF (Can\$)	4105	b - (a x c)
(e) Annual cost per patient with diabetes and HF (Can\$)	5832	a + d

### Sensitivity analysis

- Input parameters were varied, most by  $\pm 10\%$ , in one-way sensitivity analyses for the 10-year horizon

## RESULTS

### Base case

- Enalapril treatment resulted in a saving of \$1792 per patient over 5 years and \$3938 over 10 years, because of the reduced cost of treating diabetes and its complications (see Table 3)
- Over 10 years, patients receiving enalapril lived 0.414 years (151 days) longer, on average

Table 3. Model output, base case scenario\*

Outcome	With enalapril	Without enalapril	Difference (Enalapril - no enalapril)
After 5 years of treatment			
Heart failure cost (Can\$)	6,812	6,628	184
Diabetes treatment cost (Can\$)	770	2,746	-1,976
Total cost (Can\$)	7,582	9,374	-1,792
Year of life accumulated	4,228	4,123	0,105
Patients alive (%)	70.5	66.2	4.3
Patients remaining non-diabetic <sup>†</sup> (%)	90.2	65.4	22.9
After 10 years of treatment			
Heart failure cost (Can\$)	10,916	10,282	634
Diabetes treatment cost (Can\$)	2,098	6,670	-4,572
Total cost (Can\$)	13,015	16,952	-3,938
Year of life accumulated	7,187	6,773	0,414
Patients alive (%)	49.0	41.4	7.6
Patients remaining non-diabetic <sup>†</sup> (%)	82.4	45.4	37.0

\* sums and differences are subject to rounding errors  
<sup>†</sup> percentage of living patients who did not develop diabetes

### Distribution of patients in health states

- At 10 years, 40% of all enalapril-treated patients remained in the non-diabetic state, but only 19% of those not receiving enalapril did so (Figure 2)
- Of patients who remained alive at 10 years, 17% of those treated with enalapril had diabetes; 55% of those not treated with enalapril had diabetes (Figure 2 and Table 3)

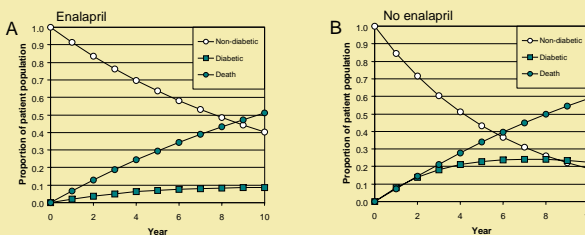


Figure 2. State probabilities for patients receiving enalapril (Panel A) or not receiving enalapril (Panel B). The probability that a patient will be in a particular state is shown for each year.

### Sensitivity analysis

- Sensitivity analyses were performed by varying input parameters, using the 10-year horizon (see Figure 3)
- The model was most sensitive to changes in probability of becoming diabetic without enalapril, cost of diabetes, and annual probability of death; changing these by 10% resulted in a change in incremental saving per patient of no more than 13%
- Increasing the discount rate from 3% to 5% changed the result by 10%
- The model was robust to variation in other parameters

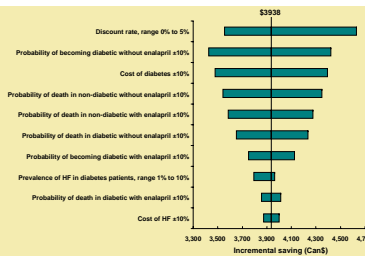


Figure 3. Sensitivity analysis for the 10-year horizon. Bars represent the change in incremental saving resulting from the indicated changes in model parameters. The vertical line indicates the base case result.

## CONCLUSIONS

- HF patients treated with enalapril incur substantially lower costs for treatment of diabetes and HF than those not treated with enalapril, because of reduced morbidity associated with diabetes
- These benefits are in addition to the morbidity and mortality benefits seen when HF patients are treated with enalapril, which has been previously shown to be cost-effective or cost-saving in these patients

## ACKNOWLEDGMENTS

The authors thank Monika Wagner of BioMedCom and Marie-Claude Meilleur of Merck Frost Canada, Ltd. for assistance and helpful discussions.

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## POTENTIAL CONFLICTS OF INTEREST

This study was funded by Merck Frost Canada Ltd., the manufacturer of enalapril. Brigitte Desjardins is an employee of Merck Frost Canada, Ltd., and participated in the study at the design and interpretation level. Derek McLachlin and Donna Rindress received consulting fees from Merck Frost Canada, Ltd. The sponsor contributed to scientific review of the study.