

# Issue with Evaluating Costs Over Time in a Context of Medical Guideline Changes: An Example in Myocardial Infarction Care Based on a Longitudinal Study from 1997 to 2018

Tania Villeneuve<sup>1</sup>  
Xavier Trudel<sup>1,2</sup>  
Mahée Gilbert-Ouimet<sup>2,3</sup>  
Jacinthe Leclerc<sup>4,5</sup>  
Alain Milot<sup>6</sup>  
Hélène Sultan-Taïeb<sup>7,8</sup>  
Chantal Brisson<sup>1,2</sup>  
Jason Robert Guertin<sup>1,2</sup> 

<sup>1</sup>Université Laval, Département de médecine sociale et préventive, Quebec City, Canada; <sup>2</sup>Centre de recherche du Centre hospitalier universitaire de l'Université Laval, Quebec City, Canada; <sup>3</sup>Université du Québec à Rimouski, Département des sciences de la santé, module des sciences infirmières, Lévis, Canada; <sup>4</sup>Université du Québec à Trois-Rivières, Département des sciences infirmières, Trois-Rivières, Canada; <sup>5</sup>Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec-Université Laval, Quebec City, Canada; <sup>6</sup>Université Laval, Département de médecine, Quebec City, Canada; <sup>7</sup>Université du Québec à Montréal (UQAM), School of Management, Montreal, Canada; <sup>8</sup>CINBIOSE, Montreal, Canada

Correspondence: Jason Robert Guertin  
Centre de recherche du CHU de Québec – Université Laval, Axe Santé des Populations et Pratiques Optimales en Santé, Hôpital du Saint-Sacrement, 1050 Chemin Ste-Foy, local J1-09B, Québec City, Québec, G1S 4L8, Canada  
Tel +1 418-682-7511, poste 82516  
Email [jason.guertin@fmed.ulaval.ca](mailto:jason.guertin@fmed.ulaval.ca)

**Background:** Cost studies appear sporadically in the scientific literature and are rarely revised unless drastic technological advancements occur. However, health technologies and medical guidelines evolve over time. It is unclear if these changes render obsolete prior estimates. We examined this issue in a cost study in the context of patients' first myocardial infarction (MI), a clinical area prone to such continuous evolution in care.

**Methods:** We conducted a longitudinal cost analysis based on a Quebec cohort. Quebec health administrative databases were used to identify incident MI cases using diagnostic codes from the international classification of diseases (ICD-9 and ICD-10). Physician fees and hospitalization costs (ie, costs incurred by the hospital center) were derived from administrative databases and a university hospital's finance department. All costs were converted to 2019 Canadian dollars. Nonparametric bootstraps were used to estimate 95% confidence intervals (CI) of the average costs of an episode of care. Generalized linear regressions were used to examine temporal trends of cost.

**Results:** Our study sample consists of 261 patients hospitalized for a first MI. The average total cost for this first event was estimated at \$5782 (95% CI: \$5293 – \$6373). Though total costs remained stable over time, physician fees increased by 123% (\$1240 vs \$2761) whereas total hospital length of stay dropped by 17% (6.6 vs 5.5 days) over the 21-year period.

**Conclusion:** Patients' first MI hospitalization impose an economic burden on the healthcare system. Though overall costs remained stable, our results suggest that some cost components varied over time.

**Keywords:** cost study, methods, observational data, myocardial infarction, longitudinal study

## Introduction

Worldwide, cardiovascular diseases cause 17.9 million deaths per year, myocardial infarction (MI) being responsible for half of them.<sup>1,2</sup> About 2.4 million Canadians were living with ischemic heart disease in 2012–2013. During this period, the MI incidence rate was 2.3 for 1000 person-years.<sup>3</sup> Considering the yearly number of events and the quantity of healthcare resources needed to manage these cases, MI are commonly regarded as a major healthcare problem.<sup>4</sup> Luckily, medical care for MI cases has evolved rapidly in the last decades; better diagnosis and rapid healthcare management have helped to decrease its mortality rate.<sup>5,6</sup>

Evolution in clinical practice and associated recommendations is often summarized within various medical associations' clinical guidelines. In Canada, the Canadian Cardiovascular Society (CCS) has published several guidelines over the last decades regarding the acute management of primary ST Elevation Myocardial Infarctions (STEMI).<sup>7–10</sup> Briefly, these guidelines reflect three main switches in treatment paradigm. Initially, Canadian guidelines favored fibrinolytic therapy as the primary MI intervention.<sup>7</sup> In the late 1990s and early 2000s,<sup>8,9</sup> Canadian guidelines moved away from fibrinolytic therapy and adopted the use of percutaneous coronary intervention (PCI) as the favored treatment option. However, more recent guidelines have changed once again and now argue that time-to-treatment is more important when deciding which of two treatments options should be favored.<sup>10,11</sup> Of note, throughout all four guidelines, CCS favored coronary artery bypass grafting (CABG) when artery reperfusion by PCI and/or fibrinolysis was impossible.

When looking at this situation in the context of a cost study, this evolution in clinical practice is particularly troublesome. Generally, cost studies appear sporadically in the scientific literature in function of requests by researchers and/or decision makers and are unfortunately rarely revised unless drastic technological advancements occur.<sup>12</sup> However, in this specific context, the various treatment options considered by these guidelines have been present for several decades. Nonetheless, it remains unclear if changes between guidelines should be viewed as a technical evolution in the care management of patients presenting a first MI or as a “drastic change” in MI practice. As such, whether historical cost data in this clinical area should be viewed as obsolete or if it should still be considered relevant remains to be clarified.

Using data from a previously established longitudinal cohort available to our team,<sup>13</sup> we aimed to quantify the healthcare resources utilized by Quebec (Canada) patients admitted in hospital for a first MI hospitalization and the related costs over a 21-year period (ie, from 1997 to 2018). Furthermore, in order to examine if healthcare resource utilization and costs changed over time, we explored if these two outcomes varied significantly between the three periods covered by these guidelines.

## Method

### Data Sources

The study population was derived from the PROspective Quebec (PROQ) Study on Work and Health led by Brisson

et al.<sup>13</sup> The initial aim of this cohort was to study the effect of psychosocial stressors at work on cardiovascular and mental health. The cohort is composed of white-collar workers of 19 public and semi-public organizations. At baseline, 9189 workers aged 18 to 65 years (mean age at baseline = 41 years) were enrolled.

In Quebec, health administrative data are systematically recorded in a centralized system, ie, the *Régie de l'assurance maladie du Québec* (RAMQ) database. This database is comprised of a series of files and two were used for the purpose of this study; the Medical Services database and the Hospital Discharge database (commonly referred to as the *Maintenance et Exploitation des Données pour l'Étude de la Clientèle Hospitalière* [MED-ECHO]). The Medical Services database was used to obtain information on physician visits (including dates and type), diagnoses, and procedures performed.<sup>14,15</sup> Diagnostic codes present in this database adhere to the International Classification of Diseases, ninth revision (ICD-9) and tenth revision (ICD-10). The Hospital Discharge database contains information about hospitalization admissions and departures in the various hospital wards (including in the intensive care unit [ICU]) as well as diagnostics and medical procedures conducted during patients' hospitalization.

Patients' records were linked across the two databases and the PROQ cohort database via the use of a unique identifier, which was encrypted to protect patient confidentiality. Ethics approval was obtained from *Centre Hospitalier Universitaire de Québec – Université Laval* (CHUdeQc-UL) ethical research committee (2012–1674; 2020–4841) and written consent was obtained by each participant of the PROQ cohort.

### Study Population

Health administrative data were available for 8781 participants of the PROQ cohort (96% of patients recruited at baseline). Patients were first selected on the basis of being admitted to a hospital with a primary diagnosis of MI between January 1, 1997 and March 31, 2018. Myocardial infarctions were identified using ICD-9 codes 410.x until March 31, 2006 and ICD-10 codes I21.x and I23.x thereafter. Only cases for whom MI was identified as the primary hospitalization diagnosis were selected. Patients' first date of admission to a hospital ward was defined as the index date and they were followed until patients' discharge from the first hospital or in-hospital death, whichever came first. Patients who died on the

index date were eligible for inclusion in the selected sample. As this study focuses on the first MI hospitalization, we excluded patients' subsequent MI hospitalizations. Additional patients' socio-demographic characteristics were obtained from data recorded in the PROQ study.

## Clinical Outcomes

Comorbidities were identified within the RAMQ databases were based on ICD-9 and ICD-10 codes<sup>16,17</sup> and are identified in [Appendix 1](#); all comorbidities were considered present if they were recorded at least once in the 365 days prior to the index date.

The Medical Services and the Hospital Discharge databases were used to identify which revascularization procedures were conducted (ie, PCI and CABG), if any, during the hospitalization. Procedures were identified with the Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCP) and the Canadian Classification of Health Intervention (CCI). In the Hospital Discharge database, PCI were identified through codes CCP 48.0, CCI 1.IJ.50 and 1.IJ.57.GQ whereas CABG were identified through codes CCP 48.1 and CCI 1.IJ.76.<sup>14,18</sup> Alternatively, PCI and CABG were identified in the Medical Services database by identifying relevant medical acts.<sup>14,15</sup> We assumed that patients underwent a PCI or a CABG procedure if any procedure code relevant to these two procedures was present in either database.

## Medical Resource Utilization

Lengths of stay in the various hospital wards were extracted from the Hospital Discharge dataset. In the event that an individual was discharged alive, transferred to another hospital or died on the index date, that individual was assigned a length of stay of one day.

## Costs

Costs occurring during patients' first MI hospitalization were examined, these included hospitalization costs (both in normal wards and ICU wards) and physician fees incurred during this hospitalization. Costs related to hospitalization were derived by multiplying the number of days spent in each ward by the yearly all-cause average daily costs (distinct costs were available for time spent in short-term wards and for time spent in the ICU). These costs included all costs incurred by the CHUdeQc-UL hospital, a university research hospital which offers various specialized care in Quebec City (Canada), over the 21-year follow-up. Nominal physician fees were identified in the Medical Services database

and were summed for each patient. All costs were converted to 2019 Canadian dollar values using the all-item consumer price index as recommended by the Canadian Agency for Drugs and Health Technologies.<sup>19,20</sup>

## Statistical Analysis

Discrete data are presented in absolute and relative (percentages) values. Continuous data are presented as mean, standard deviation (SD) and minimum and maximum or as mean and 95% confidence intervals (CI). In order, to account for the right skewed distribution of cost estimates, nonparametric bootstraps with 1000 replications were used to estimate the 95% CI around the unadjusted mean costs.

To describe the evolution of medical practice and resource utilization over time, we stratified the observation according to the date of publication of the CCS guidelines published between 1997 and 2018 (ie, 1997 to 2004 [September, 10th]; 2004 [September 11th] to 2008; 2009 to 2018) (8–10). Using these three time periods, univariate and multivariate generalized linear model (GLM) regressions were used to examine cost and resource utilization trends over time. Poisson distributions with a log link were used to fit resource utilization data whereas gamma distributions with a log link were used to fit cost data. Health resources and direct costs were adjusted for known MI risk factors most prevalent within the sample at the index date (ie, older age, male sex, tobacco use, hypertension and self-reported hyperlipidemia). Previous analyzes were also stratified according to the use of revascularization procedures during the first hospitalization to account for the evolving use of these procedures over time.<sup>8–10</sup>

An alpha value below <0.05 was used to indicate statistical significance and interpreted along with 95% CI. Statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC).

## Results

### Patients Characteristics

The final study sample is composed of 261 incident MI cases. Patients' characteristics are shown in [Table 1](#). The mean age at the time of the first MI was 61 years and 81.6% (n = 213) of cases were men. Four patients (1.5%) died during their index hospitalization; none in the 1997–2004 period, one patient (0.4%) died in the 2004–2008 period and three patients (1.2%) died in the 2009–2018 period. The most prevalent self-reported risk factors for cardiovascular disease are former or active tobacco use (62 [23.8%]) and hyperlipidemia (126 [48.3%]). Hypertension (64

**Table 1** Sociodemographic Characteristics of the Study Sample

Variable	Description
<b>Sex, n (%)</b>	
Men	213 (81.6)
Women	48 (18.4)
<b>Age in years, mean (SD)</b>	61.1 (9.7)
<b>Patients by age categories</b>	
<50	27 (10.3)
50–59	92 (35.2)
60–69	85 (32.6)
70–79	50 (19.2)
≥ 80	7 (2.7)
<b>Money income<sup>a</sup></b>	
< 40,000 \$	64 (24.8)
> 40,000 - < 60,000 \$	68 (26.4)
> 60,000 \$	126 (48.8)
<b>Tobacco use</b>	62 (23.8)
<b>Comorbidity</b>	
Self-reported hyperlipidemia	126 (48.3)
High blood pressure	64 (24.5)
Cerebrovascular disease	33 (12.6)
Diabetes	25 (9.6)
Chronic pulmonary disease	18 (6.9)
Heart failure	7 (2.7)
Renal disease	3 (1.2)
Peripheral vascular disease	1 (0.4)

Notes: <sup>a</sup>Data was missing in 1.3% of observations.

[24.5%]), cerebrovascular diseases (33 [12.6%]) and diabetes (25 [9.6%]) were the most prevalent comorbidities identified in the health administrative databases.

## Medical Resource Utilization

Medical resource utilization over the 21-year period and within each sub-period are shown in Table 2. On average, patients were hospitalized 6.0 (6.6) days due to their MI of which 4.0 (5.9) and 2.0 (2.4) days were spent on average in a short-term care and ICU ward, respectively. When

looking at the trends over time, we note that health resource utilization tended to decrease slightly over time. For example, the mean ICU length of stay dropped from 2.6 (2.3) days in the 1997–2004 period to 1.7 (1.9) days in the 2009–2018 period ( $p < 0.05$ ).

The vast majority of patients included in our study underwent a revascularization procedure ( $n = 212$  [81.2%]); this proportion rose from 50.0% ( $n = 37$ ) in the 1997–2004 period to 94.7% ( $n = 124$ ) in the 2009–2018 period (Table 2). Results also illustrate that patients who underwent a revascularization procedure had shorter total length of stays than those who did not (respectively: 5.6 [6.5] vs 7.8 [7.0] days,  $p < 0.05$ ). Though total length of stay dropped over time for patients who underwent a revascularization procedure (6.6 [4.6] vs 5.1 [5.3] days [ $p < 0.05$ ] in the 1997–2004 and 2009–2018 periods, respectively), the opposite trend was observed in patients who did not undergo a revascularization procedure (6.5 [2.6] vs 12.3 [15.6] days [ $p < 0.05$ ] in the 1997–2004 and 2009–2018 periods, respectively). Similar results were observed in the adjusted analyses (Table 3).

## Costs

Table 4 presents the unadjusted cost of patients' episode of care. Overall, patients' episode of care cost an average of \$5782 (95% CI: \$5293–\$6373). When looking at the three cost categories we examined, ICU care accounted for 39% (\$2277 [95% CI: \$1969–\$2600]), physician fees accounted for 37% (\$2166 [\$1982–\$2362]) and hospitalization in a short-term ward accounted for the remaining 23% (\$1339 [\$1115–\$1580]) of total costs. Results in Table 4 also illustrate that total costs increased over time from \$5004 (\$4464–\$5623) in the 1997–2004 period to \$6310 (\$5648–\$7010) in the 2009–2018 period ( $p < 0.05$ ). With the exception that costs related to hospitalization in a short-term ward (\$1673 [\$1127–\$2337] or 31% of total costs) were more important than physician fees (\$1082 [\$867–\$1313] or 20% of total costs) in the non-revascularized subgroup, trends observed within the unstratified population were similar to those observed within the stratified subgroups.

Adjusted costs within the three time periods are shown in Table 5. Although total costs did not differ significantly between the three periods, our results highlight that, when adjusting for the most prevalent risk factors, physician fees increased by 59% over the study period (\$1505 [\$1320–\$1715] vs \$2394 [\$2184–\$2624] in the 1997–2004 and 2009–2018 periods, respectively [ $p < 0.05$ ]). This

important increase in physician fees over time was also observed within both stratified populations.

## Discussion

Medical resources utilization and costs incurred during a patient's first hospitalization for an MI fluctuated significantly over the 21 years we studied. Though our results suggest that hospital length of stay for a first MI dropped by 17% over time (Table 2), costs, after accounting for inflation,<sup>19</sup> incurred by these same patients increased by 26% during that same period (Table 4). This increase seems to be due to physician fees which increased significantly over time (+123%). While one could expect shorter in-hospital length of stays would also lead to lower physician fees, the growing use of revascularization procedures and the overall increase in intervention-specific physician fees in Quebec during this period likely explain this observation.<sup>21,22</sup> Indeed, we observed an

impressive increase in the use of revascularization procedures amongst the hospitalized cases; going from a low of 50.0% in 1997–2004 period to a high of 94.7% in 2009–2018 period ( $p < 0.05$ ). This upward trend aligns with successive CCS guidelines that favored revascularization procedures as the gold standard in MI care management.

To the best of our knowledge, no other study has estimated resource utilization and direct cost incurred during the first MI hospitalization in Canada nor their temporal trends. However, we are aware of at least one other study conducted by a group in Alberta, Canada, that examined the annual resource utilization and costs associated with all MI cases occurring between 2004 and 2013 using claims data.<sup>23</sup> Unfortunately, the direct comparison of our results to theirs is difficult due to important methodological differences. Nevertheless, some comparisons remain noteworthy. First, like us, the authors found a slight decrease in the hospital length of stay during

**Table 2** Healthcare Resources Used by Time Categories and Stratified in Function of the Presence or Absence of a Revascularization Procedure

Healthcare Resource Use	Total	1997–2004 <sup>a</sup>	2004–2008 <sup>b</sup>	2009–2018 <sup>c</sup>
<b>Combined</b>	<b>261 (100%)</b>	<b>74 (28.4%)</b>	<b>55 (21.1%)</b>	<b>132 (50.6%)</b>
LOS in an ICU	2.0 (2.4) 0.0–22.0	2.6 (2.3) <sup>d</sup> 0.0–13.0	1.9 (3.3) 0.0–22.0	1.7 (1.9) 0.0–10.0
LOS in a short-term ward <sup>e</sup>	4.0 (5.9) 0.0–47.0	4.0 (3.8) 0.0–20.0	4.7 (7.1) <sup>d</sup> 0.0–42.0	3.8 (6.2) 0.0–47.0
Total LOS	6.0 (6.6) 1.0–64.0	6.6 (3.7) <sup>d</sup> 1.0–20.0	6.5 (9.6) <sup>d</sup> 1.0–64.0	5.5 (6.4) 1.0–47.0
<b>Intervention type<sup>f</sup></b>				
PCI	211 (80.8)	37 (50.0)	50 (90.9)	124 (93.9)
CABG	7 (2.7)	0 (0.0)	1 (1.8)	6 (4.6)
Any revascularization procedure	212 (81.2)	37 (50.0)	50 (90.9)	125 (94.7)
<b>Patients with revascularization procedure</b>				
LOS in an ICU	1.9 (2.3) 0.0–22.0	2.5 (2.1) <sup>d</sup> 0.0–7.0	1.8 (3.2) 0.0–22.0	1.7 (1.9) 0.0–10.0
LOS in a short-term ward <sup>e</sup>	3.7 (5.5) 0.0–42.0	4.1 (4.6) 0.0–20.0	4.2 (7.0) <sup>d</sup> 0.0–42.0	3.4 (5.0) 0.0–28.0
Total LOS	5.6 (6.5) 1.0–64.0	6.6 (4.6) <sup>d</sup> 1.0–20.0	6.0 (9.6) <sup>d</sup> 1.0–64.0	5.1 (5.3) 1.0–28.0
<b>Patients without a revascularization procedure</b>				
LOS in an ICU	2.5 (2.6) 0.0–13.0	2.6 (2.6) 0.0–13.0	2.6 (4.0) 0.0–9.0	2.0 (2.0) 0.0–5.0
LOS in a short-term ward <sup>e</sup>	5.3 (7.3) 0.0–47.0	3.9 (2.8) <sup>d</sup> 0.0–10.0	8.8 (8.5) 0.0–21.0	10.3 (16.6) 0.0–47.0
Total LOS	7.8 (7.0) 2.0–47.0	6.5 (2.6) <sup>d</sup> 3.0–13.0	11.4 (9.5) 2.0–22.0	12.3 (15.6) 4.0–47.0

**Notes:** Results are presented as mean (standard deviation) and minimum – maximum number of days, unless noted. <sup>a</sup>01-01-1997 – 10-09-2004. <sup>b</sup>11-09-2004 – 31-12-2008. <sup>c</sup>01-01-2009 – 31-03-2018. <sup>d</sup>p-value < 0.05; comparison made to values in the 2009–2018 period. <sup>e</sup>Excluding the length of stays in the ICU, when applicable. <sup>f</sup>Some patients underwent both a PCI and a CABG during the same hospitalization.

**Abbreviations:** ICU, intensive care units; LOS, length of stay.

**Table 3** Adjusted Healthcare Resources Used (95% Confidence Intervals) by Time Categories and in Function of the Presence or Absence of a Revascularization Procedures

Healthcare Resource	1997–2004 <sup>a</sup>	2004–2008 <sup>b</sup>	2009–2018 <sup>c</sup>
LOS in an ICU	2.4 (2.0–2.9) <sup>d</sup>	1.9 (1.6–2.3)	1.7 (1.5–1.9)
LOS in a short-term ward <sup>e</sup>	4.0 (3.4–4.6)	4.8 (4.2–5.4) <sup>d</sup>	3.5 (3.1–3.9)
Total LOS	6.5 (5.8–7.2) <sup>d</sup>	6.8 (6.1–7.5) <sup>d</sup>	5.2 (4.8–5.7)
<b>With a revascularization procedure</b>			
LOS in an ICU	2.5 (2.0–3.1) <sup>d</sup>	1.8 (1.4–2.2)	1.7 (1.4–1.9)
LOS in a short-term ward <sup>e</sup>	4.5 (3.8–5.4) <sup>d</sup>	4.3 (3.8–5.0) <sup>d</sup>	3.2 (2.9–3.5)
Total LOS	7.2 (6.3–8.2) <sup>d</sup>	6.2 (5.5–6.9) <sup>d</sup>	4.9 (4.5–5.3)
<b>Without a revascularization procedure</b>			
LOS in an ICU	2.4 (1.9–3.0)	3.1 (1.8–5.5)	2.1 (1.1–3.9)
LOS in a short-term ward <sup>e</sup>	3.7 (3.1–4.5)	6.1 (4.4–8.6)	5.4 (3.6–8.0)
Total LOS	6.4 (5.6–7.3)	9.7 (7.2–12.9)	8.6 (6.2–11.8)

**Notes:** Average results (95% CI) adjusted for: sex, age, tobacco use, self-reported hyperlipidemia, hypertension, time periods, presence or absence of a revascularization procedure. <sup>a</sup>01-01-1997 – 10-09-2004. <sup>b</sup>11-09-2004 – 31-12-2008. <sup>c</sup>01-01-2009 – 31-03-2018. <sup>d</sup>p-value < 0.05; comparison made to the 2009–2018 reference period. <sup>e</sup>Excluding the length of stays in the ICU, when applicable.

**Abbreviations:** ICU, intensive care units; LOS, length of stay.

**Table 4** Myocardial Infarction Cost (95% Confidence Intervals) by Cost Categories Over Time and in Function of the Presence or Absence of Revascularization Procedures

Cost Categories	Total	1997–2004 <sup>a</sup>	2004–2008 <sup>b</sup>	2009–2018 <sup>c</sup>
ICU	2277 (1969–2600)	2565 (2067–3171)	2086 (1249–3125)	2195 (1773–2606)
Short-term hospital ward	1339 (1115–1580)	1199 (949–1479)	1492 (955–2143)	1354 (1015–1737)
Physician fees	2166 (1982–2362)	1240 (1116–1366) <sup>d</sup>	1984 (1607–2499) <sup>d</sup>	2761 (2513–3043)
Total cost	5782 (5293–6373)	5004 (4464–5623) <sup>d</sup>	5563 (4046–7574)	6310 (5648–7010)
<b>With revascularization procedure</b>				
ICU	2209 (1870–2581)	2625 (1985–3302)	1995 (1228–3088)	2172 (1740–2599)
Short-term hospital ward	1262 (1033–1515)	1248 (855–1737)	1349 (841–1987)	1231 (938–1574)
Physician fees	2417 (2224–2648)	1647 (1536–1764) <sup>d</sup>	2000 (1596–2562) <sup>d</sup>	2812 (2555–3109)
Total cost	5888 (5312–6571)	5520 (4775–6383)	5343 (3884–7511)	6215 (5513–6906)
<b>Without revascularization procedure</b>				
ICU	2569 (1826–3401)	2505 (1727–3431)	2999 (0–7216)	2598 (604–4847)
Short-term hospital ward	1673 (1127–2337)	1150 (872–1432)	2929 (675–5544)	3544 (617–8362)
Physician fees	1082 (867–1313)	833 (700–981) <sup>d</sup>	1830 (953–2895)	1862 (1026–3218)
Total cost	5324 (4348–6413)	4488 (3736–5395) <sup>d</sup>	7759 (2963–14,029)	8005 (4806–13,401)

**Notes:** <sup>a</sup>01-01-1997 – 10-09-2004. <sup>b</sup>11-09-2004 – 31-12-2008. <sup>c</sup>01-01-2009 – 31-03-2018. <sup>d</sup>p-value < 0.05; comparison made to the 2009–2018 reference period.

**Abbreviation:** ICU, intensive care unit.

**Table 5** Adjusted Average Myocardial Infarction Cost (95% Confidence Interval) by Cost Categories Over Time and in Function of the Presence or Absence of Revascularization Procedures

Cost Categories	1997–2004 <sup>a</sup>	2004–2008 <sup>b</sup>	2009–2018 <sup>c</sup>
ICU	2503 (1399–4477)	2121 (1175–3831)	2149 (1411–3271)
Short-term hospital ward	1357 (775–2376)	1473 (872–2488)	1173 (797–1725)
Physician fees	1505 (1320–1715) <sup>d</sup>	1912 (1683–2173) <sup>d</sup>	2394 (2184–2624)
Total cost	5405 (4591–6364)	5633 (4795–6617)	5939 (5291–6665)
<b>With revascularization procedure</b>			
ICU	2706 (1246–5877)	1987 (1056–3739)	2106 (1391–3188)
Short-term hospital ward	1509 (715–3188)	1364 (762–2441)	1096 (745–1613)
Physician fees	1775 (1503–2095) <sup>d</sup>	2040 (1785–2333) <sup>d</sup>	2697 (2470–2945)
Total cost	5981 (4825–7413)	5418 (4561–6436)	5977 (5336–6694)
<b>Without revascularization procedure</b>			
ICU	2407 (1222–4738)	3390 (460–26,970)	2479 (369–16,675)
Short-term hospital ward	1267 (740–2170)	1801 (413–7857)	1441 (329–6313)
Physician fees	847 (738–971) <sup>d</sup>	1514 (1045–2194)	1345 (944–1918)
Total cost	4514 (3827–5324)	6783 (4286–10,734)	6776 (4453–10,310)

**Notes:** Results adjusted for: sex, age, tobacco use, self-reported hyperlipidemia, hypertension, time periods, presence or absence of a revascularization procedure. <sup>a</sup>01-01-1997 – 10-09-2004. <sup>b</sup>11-09-2004 – 31-12-2008. <sup>c</sup>01-01-2009 – 31-03-2018. <sup>d</sup>p-value < 0.05; comparison made to the 2009–2018 reference period.

**Abbreviation:** ICU, intensive care unit.

their study period (median [interquartile range] length of stay = 7 days [4–10] in 2004 vs 5 [3–7] days in 2013,  $p < 0.001$ ). Secondly, unlike us, their results indicate that the per patient average hospitalization cost dropped from \$14,116 in 2004 to \$11,792 in 2013 ( $p < 0.001$ ). That being said, it is important to note that this decrease was not constant over time; for example, the highest average per patient cost of \$14,219 was observed in 2008 (no comparisons were provided by the authors). Finally, though they report an increase in total annual physician fees over time, no relevant breakdown facilitating the comparison between their study and ours is provided. It is therefore impossible to identify if, like in our study, increasing physician fees offset the decrease in hospitalization cost they observed.

## Strengths and Limitations

We believe our study has many strengths. Bringing novelty, we had access to data from the PROQ study, a prospective cohort which was established in Quebec City over 25 years ago,<sup>13</sup> that was linked to the Quebec

claims data. Using these combined datasets, we were able to examine resource utilization and associated costs of incident MI cases occurring between 1997 and 2018. Though others have examined a greater number of patients using only claims data,<sup>23</sup> we were able to minimize the possibility of confounding bias by the use of our combined dataset, which granted us the option of adjusting for various socio-demographic characteristics which are normally unavailable within claims data (eg, tobacco use) and allowed us to better account for structural changes in MI care.<sup>8–10</sup> Furthermore, through collaboration with the CHU de Québec-Université Laval, Quebec City's primary hospital network, we were able to obtain the average all-cause daily hospitalization costs throughout the 21-year follow-up. Using this data allowed us to more accurately account for the effect of inflation over this 21-year period and therefore better highlight the evolution in hospital costs over time. Unfortunately, the hospitalization costs specific to the cardiology ward were not available. Future studies examining this or a similar topic should aim to obtain more precise cost estimates in order to even better account

for potentially fluctuating costs within disease areas and/or case-mix groups.<sup>20</sup>

Still, our study has limitations. First, healthcare resource utilization was based on retrospective data that is updated over time. As coding habits may evolve, some misclassifications cannot be fully excluded. In addition, we could not account for any diagnostic errors and misclassification bias within the databases, which could lead to under or over-estimation of MI cases and related costs.<sup>24–26</sup> Second, the fact that our study is limited to 261 cases identified from a cohort of 8781 white-collar workers in the greater Quebec City area could limit the external validity of our results. For example, the high proportion of cases who underwent revascularization procedures in our cohort may be due to the fact that Quebec City houses two university hospitals, including a specialized Cardiology center (ie, the Quebec Heart and Lung Institute). Results regarding the average cost of the first MI hospitalization we observed could be different in other regions (eg, rural settings) but the methodological issue we identified (ie, the non-constant change in cost) should remain.<sup>27</sup> Third, our adjusted results may be biased by some residual confounding. Due to our sample size, we could only adjust for the most prevalent risk factors in our multivariate analyses. Had our sample size been greater, we would have wanted to include additional factors in our regression model (eg, patients' diabetes status) and/or stratify results by patients' biological sex and MI subtypes (STEMI vs NSTEMI).<sup>28</sup> Fourth, despite the quality of data contained within the PROQ cohort,<sup>13</sup> data regarding three socio-demographic characteristics were missing in up to 1.3% of patients (Table 1). Nonetheless, impact of this missing data was limited since these variables were not used in any subsequent analyses. Finally, we categorized time periods in function of the date when the CCS published their revised recommendations.<sup>8–10</sup> We cannot exclude the fact that these groupings may be too inclusive or may incorrectly account for changes in practice. For example, clinicians' uptake of these guidelines may not occur systematically on the day of publication of these recommendations and they may also be influenced by other American and international guidelines (eg,<sup>29–31</sup>). Furthermore, such broad groupings may also incorrectly reflect “non-drastic technological changes” that affect the cost of care but not its quality. For example, we cannot exclude the possibility that at least some of the post-inflation increase in physician fees we observed was due to physician fee negotiations which should have no impact on the quality of care. Other potential factors include drug

price negotiations and patent loss for drugs and stents.<sup>20,32</sup> Had we had a greater number of observations and more granular cost data, we would have wanted to examine these trends by grouping the data into shorter time periods (eg, yearly or quarterly) and attempt to account for these factors within our adjusted models.

## Conclusion

Overall, we found that hospitalizations for the first MI cost an average of \$5782 to the Quebec healthcare system. However, our results illustrate that costs have varied over time. Specifically, over 21 years, these costs increased from a low of \$5004 to a high of \$6310. Although we cannot state that these variations were due in full or in part to the evolution in MI-related medical management, we believe that future work should further examine this hypothesis.

From a broader methodological perspective, such results are problematic. Seeing as cost studies are relatively rare and infrequent, it is likely that this issue and similar ones are involuntarily ignored in many cases when researchers actualize older cost data or group together data from long-term longitudinal studies. Teams conducting future cost studies should be encouraged to not only provide total cost estimates but to also provide more granular cost data (eg, stratify the cost data by sub-components). By doing so, it may be easier for future teams referencing these estimates to account for various technological changes that only affect specific cost sub-components (eg, physician fee negotiations).

## Funding

Work presented in this manuscript was funded by the Réseau québécois de recherche sur les médicaments (RQRM), a thematic network supported by the Fonds de recherche du Québec-Santé; the funding agreements ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report. MGO holds the Chaire de recherche du Canada sur le sexe et le genre en santé au travail. JRG is the recipient of a Chercheur-boursier Junior 1 career award from the Fonds de recherche du Québec-Santé (FRQS #266460).

## Disclosure

Part of the work presented in this manuscript formed the basis of the first author's, Ms. Tania Villeneuve, master's thesis. Dr Alain Milot reports grants from Novo Nordisk, grants from Bayer, grants from Eli Lilly, outside the submitted work. Dr Chantal Brisson reports grants from



Canadian Institute of Health Research, during the conduct of the study. The authors report no other conflicts of interest in this work.

## References

1. Finegold JA, Asaria P, Francis DP. Mortality from ischaemic heart disease by country, region, and age: statistics from World Health Organisation and United Nations. *Int J Cardiol.* 2013;168(2):934–945. doi:10.1016/j.ijcard.2012.10.046
2. World Health Organisation. The top 10 causes of death 2020. Available from: <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death>. Accessed December 21, 2021.
3. Public Health Agency of Canada. *Report from the Canadian Chronic Disease Surveillance System: Heart Disease in Canada*. Ottawa (Ontario): Public Health Agency of Canada; 2018. Report No.: 170308.
4. Mendis S, Thygesen K, Kuulasmaa K, et al. World Health Organization definition of myocardial infarction: 2008–09 revision. *Int J Epidemiol.* 2011;40(1):139–146. doi:10.1093/ije/dyq165
5. Hunink MGM, Goldman L, Tosteson ANA, et al. The recent decline in mortality from coronary heart disease, 1980–1990: the effect of secular trends in risk factors and treatment. *JAMA.* 1997;277(7):535–542. doi:10.1001/jama.1997.03540310033031
6. Tu JV, Nardi L, Fang J, et al. National trends in rates of death and hospital admissions related to acute myocardial infarction, heart failure and stroke, 1994–2004. *CMAJ.* 2009;180(13):E118–25. doi:10.1503/cmaj.081197
7. Canadian Cardiovascular Society. *1992 Canadian Consensus Conference on Coronary Thrombolysis*; 1992.
8. Canadian Cardiovascular Society. *Indications for and Access to Revascularization*; 1995.
9. Armstrong PW, Bogaty P, Buller CE, Dorian P, O'Neill BJ. The 2004 ACC/AHA Guidelines: a perspective and adaptation for Canada by the Canadian Cardiovascular Society Working Group. *Can J Cardiol.* 2004;20(11):1075–1079.
10. Welsh RC, Travers A, Huynh T, Cantor WJ. Canadian Cardiovascular Society Working Group: providing a perspective on the 2007 focused update of the American College of Cardiology and American Heart Association 2004 guidelines for the management of ST elevation myocardial infarction. *Canadian J Cardiol.* 2009;25(1):25–32. doi:10.1016/S0828-282X(09)70019-4
11. de Boer Sanneke PMS, Barnes EH, Westerhout CM. High-risk patients with ST-elevation myocardial infarction derive greatest absolute benefit from primary percutaneous coronary intervention: results from the Primary Coronary Angioplasty Trialist versus thrombolysis (PCAT)-2 collaboration. *Am Heart J.* 2011;161(3):500–507. doi:10.1016/j.ahj.2010.11.022
12. Drummond M, Sculpher M, Claxton K, Stoddart G, Torrance G. *Methods for the Economic Evaluation of Health Care Programmes*. 4 ed. Oxford: Oxford University Press; 2015.
13. Trudel X, Gilbert-Ouimet M, Milot A, et al. Cohort Profile: the PROspective Quebec (PROQ) Study on Work and Health. *Int J Epidemiol.* 2018;47(3):693–693i. doi:10.1093/ije/dyy026
14. Régie de l'assurance maladie du Québec. Manuel des médecins omnipraticiens – rémunération à l'acte 2021. Available from: <https://www.ramq.gouv.qc.ca/SiteCollectionDocuments/professionnels/manuels/syra/medecins-omnipraticiens/100-facturation-omnipraticiens/manuel-omnipraticiens-remuneration-acte.html>. Accessed December 21, 2021.
15. Régie de l'assurance maladie du Québec. Manuel des médecins spécialistes – rémunération à l'acte 2021. Available from: <https://www.ramq.gouv.qc.ca/SiteCollectionDocuments/professionnels/manuels/syra/medecins-specialistes/150-facturation-specialistes/manuel-specialistes-remuneration-acte.html>. Accessed December 21, 2021.
16. Quan H, Khan N, Hemmelgarn BR, et al. Validation of a case definition to define hypertension using administrative data. *Hypertension.* 2009;54(6):1423–1428. doi:10.1161/HYPERTENSIONAHA.109.139279
17. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care.* 2005;43(11):1130–1139. doi:10.1097/01.mlr.0000182534.19832.83
18. Ministère de la Santé et des Services sociaux. Cadre normatif du système MED-ÉCHO - Mise à jour 2021 2021. Available from: <https://publications.msss.gouv.qc.ca/msss/document-000170/>. Accessed December 21, 2021.
19. Statistics Canada. Table 18- 10-0005-01 Consumer Price Index, annual average, not seasonally adjusted 2020. Available from: <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1810000501>. Accessed December 21, 2021.
20. CADTH. *Guidance Document for the Costing of Health Care Resources in the Canadian Setting*. 2nd ed. Ottawa: CADTH; 2016.
21. Contandriopoulos D, Perroux M. Fee increases and target income hypothesis: data from Quebec on physicians' compensation and service volumes. *Health Policy.* 2013;9(2):30–35.
22. Hébert G. *La rémunération des médecins québécois*. IRIS; 2016.
23. Tran DT, Ohinmaa A, Thanh NX, Welsh RC, Kaul P. The Healthcare Cost Burden of Acute Myocardial Infarction in Alberta, Canada. *Pharmacoecon Open.* 2018;2(4):433–442. doi:10.1007/s41669-017-0061-0
24. Lambert L, Blais C, Hamel D, et al. Evaluation of Care and Surveillance of Cardiovascular Disease: can We Trust Medico-administrative Hospital Data? *Canadian J Cardiol.* 2012;28(2):162–168. doi:10.1016/j.cjca.2011.10.005
25. Robitaille C, Bancej C, Dai S, et al. Surveillance of ischemic heart disease should include physician billing claims: population-based evidence from administrative health data across seven Canadian provinces. *BMC Cardiovasc Disord.* 2013;13:88. doi:10.1186/1471-2261-13-88
26. Wilchesky M, Tamblyn RM, Huang A. Validation of diagnostic codes within medical services claims. *J Clin Epidemiol.* 2004;57(2):131–141. doi:10.1016/S0895-4356(03)00246-4
27. Wong GC, Welsford M, Ainsworth C, et al. 2019 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Guidelines on the Acute Management of ST-Elevation Myocardial Infarction: focused Update on Regionalization and Reperfusion. *Can J Cardiol.* 2019;35(2):107–132. doi:10.1016/j.cjca.2018.11.031
28. Roggeri A, Gnani R, Dalmaso M, et al. Resource consumption and healthcare costs of acute coronary syndrome: a retrospective observational administrative database analysis. *Crit Pathw Cardiol.* 2013;12(4):204–209. doi:10.1097/HPC.0b013e3182a78c06
29. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2013;127(4):529–555. doi:10.1161/CIR.0b013e3182742c84
30. Antman EM, Anbe DT, Armstrong PW. ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. *Circulation.* 2004;110(9).
31. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018;39(2):119–177. doi:10.1093/eurheartj/ehx393
32. Guertin JR, Mitchell D, Ali F, LeLorier J. Bias within economic evaluations - the impact of considering the future entry of lower-cost generics on currently estimated incremental cost-effectiveness ratios of a new drug. *Clinicoecon Outcomes Res.* 2015;7:497–503. doi:10.2147/CEOR.S90386

### ClinicoEconomics and Outcomes Research

Dovepress

#### Publish your work in this journal

ClinicoEconomics and Outcomes Research is an international, peer-reviewed open-access journal focusing on Health Technology Assessment, Pharmacoeconomics and Outcomes Research in the areas of diagnosis, medical devices, and clinical, surgical and pharmacological intervention. The economic impact of health policy and health systems

organization also constitute important areas of coverage. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/clinicoeconomics-and-outcomes-research-journal>