



## TEN-YEAR STATIN ADHERENCE IN SURVIVORS OF ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION: INSIGHTS FROM THE AMI-QUEBEC STUDY

T Huynh<sup>1</sup>, P Lecca<sup>1</sup>, M Montigny<sup>2</sup>, R Gagnon<sup>1</sup>, M Eisenberg<sup>3</sup>, C Lauzon<sup>5</sup>, S Mansour<sup>6</sup>, S Rinfret<sup>1</sup>, M Afilalo<sup>4</sup>, M Nguyen<sup>7</sup>, S Kouz<sup>8</sup>, JP Déry<sup>9</sup>, R Harvey<sup>7</sup>, E Schampaert<sup>10</sup>, and J-C Tardif<sup>11</sup>

<sup>1</sup>McGill Health University Center, <sup>2</sup>Cité de la Santé de Laval, <sup>3</sup>Jewish General Hospital, <sup>4</sup>Centre Hospitalier de l'Amiante, <sup>5</sup>Centre Hospitalier de l'Université de Montréal, <sup>6</sup>Centre Hospitalier Universitaire de Sherbrooke, <sup>7</sup>Centre Hospitalier Régional de Joillette, <sup>8</sup>Institut Universitaire de Cardiologie et de Pneumologie de Québec, <sup>9</sup>Hopital du Sacre-Coeur de Montreal, <sup>10</sup>Institute de Cardiologie de Montreal

Corresponding author Thao Huynh [Thao.huynhthanh@mcgill.ca](mailto:Thao.huynhthanh@mcgill.ca)

Submitted: December 1, 2017. Accepted: October 25, 2018. Published: November 6, 2018.

---

### ABSTRACT

#### Background

Adherence to statins is often sub-optimal and declines over time. Direct costs incurred by patients are often cited as responsible for inadequate statin adherence. To determine whether patients with ST-segment elevation myocardial infarction (STEMI) who benefit from low or no-cost drug dispensation have optimal long-term adherence to statins, we aimed to evaluate 10-year adherence to statin in a cohort of STEMI survivors.

#### Methods

The AMI-QUEBEC Study follows a cohort of STEMI patients hospitalized at 17 hospitals in Quebec, Canada during the year 2003. We obtained 10-year data on lipid lowering therapy (LLT) consumption in STEMI survivors with drug coverage by the Quebec Provincial Health Board (i.e., Régie de l'Assurance Maladie du Québec – RAMQ). Optimal adherence was defined as the proportion of days covered (PDC) of  $\geq 80\%$ . We used multivariate logistic regression to determine factors independently associated with optimal adherence to statins.

#### Results

Complete 10-year data on statin dispensation was available for 524 patients. Optimal adherence remained stable over time at 80% and more during the 10-year follow-up period. During the last 5 years, despite

being STEMI patients at very high-risk and therefore requiring some LLT therapy, 12% of patients did not use any LLT. Patients between the age of 60 and 80 years had the most optimal PDC. Older age (up to 80 years), living in less socially deprived areas, concomitant use of angiotensin-converting-enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), and admission to percutaneous coronary interventions (PCI)-hospitals were associated with improved statin adherence.

### Conclusion

Future studies are needed to explore the potential factors associated with concomitant use of ACEI/ARB, and admission to PCI-hospitals that may have optimized statin adherence. As for socially deprived patients (single, widow, single-parent family member, and those who lived alone), they may benefit from more support and encouragement to enhance their long-term statin adherence.

### Keywords: Adherence, Statins, Myocardial Infarction

Although the benefits of statins in reducing major cardiovascular adverse events following acute myocardial infarction have been well established,<sup>1</sup> utilization and adherence to statins is often sub-optimal and declines over time.<sup>2-6</sup> Poor adherence to statins has been associated with increased risks of repeat hospitalizations, cardiovascular (CV) events and increased medical costs.<sup>3,7-13</sup> Adherence is generally higher in individuals with high mortality risks compared to those at lower mortality risks.<sup>16-18</sup> Reuter et al. showed that 88% of survivors of ST-segment elevation myocardial infarction (STEMI) were still taking statins at 36-month.<sup>18</sup> However, very limited data is available regarding longer term statin adherence.

Factors associated with poor adherence to statins are numerous and include age, adverse events, co-payment, socio-economic factors, new statin use, primary prevention, co-morbidities, and concomitant medications.<sup>16-17,19-21</sup> Direct costs incurred by patients are often cited as responsible for non- to poor adherence to statins.<sup>16-17,19-21</sup> In Quebec (Canada), permanent residents who are 65 years and older benefit from a comprehensive governmental drug coverage whereby all subjects can receive statins with no or very low copayments required. Depending on net family income, annual premiums vary from \$0 to \$660 and monthly co-payment can be nil or up to 34.5% of drug cost to a maximum of \$86.<sup>22</sup> Even though the consequences of their non-adherence can be life-threatening,<sup>3-13</sup> it remains unclear whether patients with STEMI who benefit from low/no-cost drug dispensation have optimal long-term adherence to statins. We aimed to evaluate 10-year adherence to statin in STEMI survivors in Quebec, Canada.

## METHODS

### Study Cohort

The Acute Myocardial Infarction (AMI)-QUEBEC Study is an observational cohort study of patients with a primary discharge diagnosis of STEMI admitted at 17 participating hospitals in the province of Quebec from January 1<sup>st</sup> to December 31<sup>st</sup>, 2003. The details of this study have been previously described.<sup>23</sup>

We linked the AMI-QUEBEC data set with the provincial administrative databases. We performed data linkage by matching patients in the provincial administrative databases with patients enrolled in the AMI-QUEBEC study based on initials, birthdates, sex, admitting hospitals and dates of STEMI. The health provincial data sets used were those of the provincial medical insurance board (Régie de l'Assurance Maladie du Québec (RAMQ)), the Quebec Civil Status Registry which records deaths (deaths registered in the Registre de l'État Civil du Québec) and the provincial hospitalization records (MedECHO).

For the purposes of this study, we included only patients who fulfilled all of the following criteria: (1) survived the index STEMI, (2) health information could be retrieved from the provincial administrative data sets between April 1<sup>st</sup> 2003 to March 31<sup>st</sup> 2013, (3) drug coverage by the RAMQ (as shown by at least one medication dispensation during the first year after the index STEMI) and (4) received at least one dose of statin between the index STEMI and March 31<sup>st</sup>, 2013. The study received approval of the ethics board of the coordinating hospital (McGill Health University Center), Commission d'Accès à l'Information

(Provincial Board of Access to Information) and the directors of professional services of all the participating hospitals. (Appendix 1).

### Study Variables

All the baseline characteristics were captured at the time of the index STEMI. We evaluated adherence by calculating the proportion of days covered (PDC), which was defined by the total length of statin therapy in days divided by the number of days of follow-up. Optimal adherence was defined as a PDC of  $\geq 80\%$ . The validity of PDC and its cut-off of 80% had been validated to evaluate adherence to medications.<sup>13,14</sup> Patients were considered adherent if their PDC was  $\geq 80\%$  during the whole follow-up period (excluding hospitalizations, when they would have received in-hospital statin dispensation). For patients with non-persistence to statins, we stopped measuring PDC after the last statin dispensation during the 10-year follow-up. Therefore, we measured PDC only while patients were still taking the statins. Follow-up period was defined as the period from the day of discharge after the index STEMI to the occurrence of either death or the end of the study (March 31, 2013), whichever occurred earlier.

High-potency statins were defined as either atorvastatin  $\geq 40$  mg, rosuvastatin  $\geq 20$  mg or simvastatin 80 mg. All other types and doses of statin were considered of low/moderate potency. All other non-statin lipid-lowering therapies (LLT) (ezetimibe, fibrates, colestipol) were analyzed together.

We used the Quebec's National Public Health Institute (Institut National Santé Public du Québec (INSPQ)) deprivation index to evaluate material and social deprivation. This index was constructed based on information from the most current Census Canada for the enumeration area of patients' residences.<sup>24</sup> The deprivation index consists of six socio-economic indicators. Material deprivation was based on (1) proportion of people aged 15 years and older with no high school diploma, (2) population/employment ratio of people aged 15 years and older and (3) average income of people aged 15 years and older. Social deprivation was based on (1) proportion of individuals aged 15 years and older living alone, (2) proportion of individuals aged 15 years and older whose marital status is either separated, divorced, or widowed and (3) proportion of

single-parent families. Each enumeration area received a score separately for material and social deprivation. The scores were further stratified into quintiles with Quintile 1 (Q1) representing the least deprived, and Quintile 5 (Q5) being the most deprived. For this study, RAMQ provided the material and social deprivation quintiles for all of the patients included in our cohort.

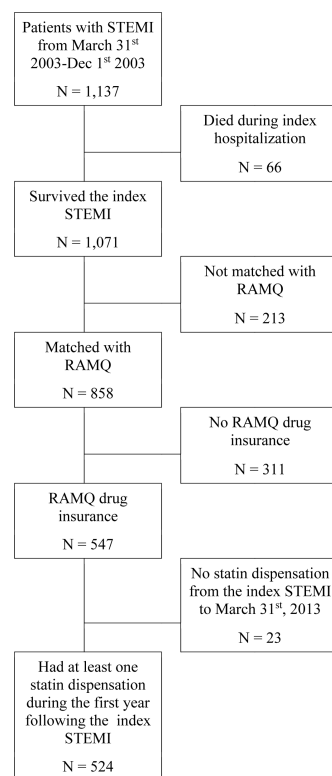
### Statistical Analyses

We used Student's t-test for comparison of continuous variables and chi-squared tests for categorical variables between adherent and non-adherent patients. Multivariate logistic regression was used to identify patient characteristics associated with statin adherence. For both models, the variables were selected using a stepwise algorithm with a significance level of 0.30 for entry and a significance level of 0.10 for inclusion. All analyses were done with SAS Enterprise Guide 7.1.

## RESULTS

Figure 1 shows the final inclusion of patients. Of the 1,071 patients who survived the index STEMI,

**FIG. 1** Flowchart of inclusion and exclusion of patients.



there were 858 patients with successfully retrieved long-term health data from the provincial health data sets. We further excluded 311 patients who did not have drug insurance with the RAMQ. Then, we excluded 23 patients who did not receive any statin during the study period. The final study cohort was composed of 524 patients who filled at least 1-month supply of statin following the index STEMI. Of this cohort, 475 (91%) were still alive at 10 years.

The mean age of the study cohort was 64 years and 32% were females; 13% of patients had diabetes mellitus and 22% had prior CV events (Table 1). Seventy-two percent of patients filled their statin prescription on the day of hospital discharge and 81% of patients filled their prescription within the first month of hospital

discharge (Figure 2). Ten percent of patients filled their statin prescription more than 5 months after the index STEMI (4% beyond one year). During the first five years, LLT was dispensed in most patients (99%); this proportion declined to 88% during the last 5 years (Figure 3). Statins were the predominant type of LLT (89% and 78% of patients, during the first 5 years and during the last 5 years, respectively) (Figure 3). Non-statin LLT were used in approximately 10% of patients and mostly in combination with statins. High-potency statins (with/without other types of LLT) were infrequently used with only 8% of patients who received statin at discharge of the index STEMI and 36% of patients who received statin at the last dispensation during the 10-year follow-up (Figure 4).

**TABLE 1** Baseline Characteristics of All Patients, Adherent and Non-adherent Patients

	<b>All Patients N=524 (%)</b>	<b>Adherent N=340 (%)</b>	<b>Non-adherent N=184 (%)</b>	<b>p-values*</b>
<b>Mean age, years (SD)</b>	64.1 (12.6)	65.3 (11.4)	61.8 (14.2)	0.0002
<b>Female, n (SD)</b>	169 (32.3)	112 (34.5)	57 (28.6)	0.30
<b>Beneficiaries of guaranteed income supplement</b>	114 (21.8)	80 (23.5)	34 (18.5)	0.18
<b>Material deprivation</b>				
1 (least deprived)	101 (19.3)	61 (17.9)	40 (21.7)	0.47
2	92 (17.6)	58 (17.1)	34 (18.5)	
3	91 (17.4)	62 (18.9)	29 (15.8)	
4	104 (20.0)	71 (20.9)	33 (17.9)	
5 (most deprived)	116 (22.1)	76 (22.4)	40 (21.7)	
<b>Social deprivation</b>				
1 (least deprived)	84 (16.0)	59 (17.4)	25 (13.6)	0.02
2	92 (17.6)	71 (20.9)	21 (11.4)	
3	101 (19.3)	63 (18.5)	38 (20.6)	
4	111 (21.2)	72 (21.2)	39 (21.2)	
5 (most deprived)	116 (22.1)	63 (18.5)	53 (28.8)	
<b>Diabetes Mellitus</b>	69 (13.2)	49 (14.4)	20 (10.9)	0.25
<b>Prior CV event</b>	113 (21.6)	76 (22.4)	37 (20.1)	0.56
<b>Anterior MI</b>	243 (46.4)	157 (46.1)	86 (47.7)	0.90

**TABLE 1** Baseline Characteristics of All Patients, Adherent and Non-adherent Patients (*Continued*)

	<b>All Patients N=524 (%)</b>	<b>Adherent N=340 (%)</b>	<b>Non-adherent N=184 (%)</b>	<b>p-values*</b>
<b>Killip class &gt;1</b>	78 (14.9)	53 (16.0)	25 (14.0)	0.53
<b>Baseline clearance creatinine (ml/min) (n=472)</b>	79.8 (30.6)	78.8 (30.9)	81.7 (30.2)	0.80
<b>Mean GRACE score (SD)</b>	143.8 (40.9)	147.1 (41.5)	137.8 (39.2)	0.01
<b>Mean LVEF (SD)</b>	48.3 (11.6)	47.2 (12.1)	50.2 (10.6)	0.006
<b>Median TIMI score (Q1, Q3)</b>	2.5(0,4)	2.7 (2,5)	2.0 (0,4)	0.02
<b>Mean TRI index (SD)</b>	23.9 (12.9)	25.0 (12.3)	21.9 (15.0)	0.009
<b>Hospital with on-site PCI facility</b>	362 (69.1)	249 (73.2)	113 (61.4)	0.005
<b>In-hospital PCI</b>	390 (74.4)	261 (76.6)	129 (70.1)	0.10
<b>Major in-hospital CV event during the index hospitalization</b>	74 (14.2)	49 (14.4)	25 (13.36)	0.79
Major bleeding	37 (7.1)	24 (7.1)	13 (7.1)	1.00
Heart failure	37 (7.1)	23 (6.8)	14 (7.6)	0.72
Reinfarction	13 (2.5)	10 (2.9)	3 (1.6)	0.34
Stroke	2 (0.4)	2 (0.6)	0 (0.0)	0.30
<b>Discharge prescription</b>				
ACEI and/or ARB	401 (76.5)	278 (81.8)	123 (66.9)	0.0001
Aspirin	480 (91.6)	314 (92.4)	166 (90.2)	0.40
Aspirin and thienopyridines	382 (72.9)	255 (75.0)	127 (69.0)	0.14
Beta blocker	449 (85.7)	296 (87.1)	153 (83.2)	0.22
Calcium channel blocker	27 (5.2)	18 (5.3)	9 (5.0)	0.84
Lipid lowering therapy	426 (81.3)	286 (84.1)	140 (76.1)	0.02

\*Comparison between adherent and non-adherent patients.

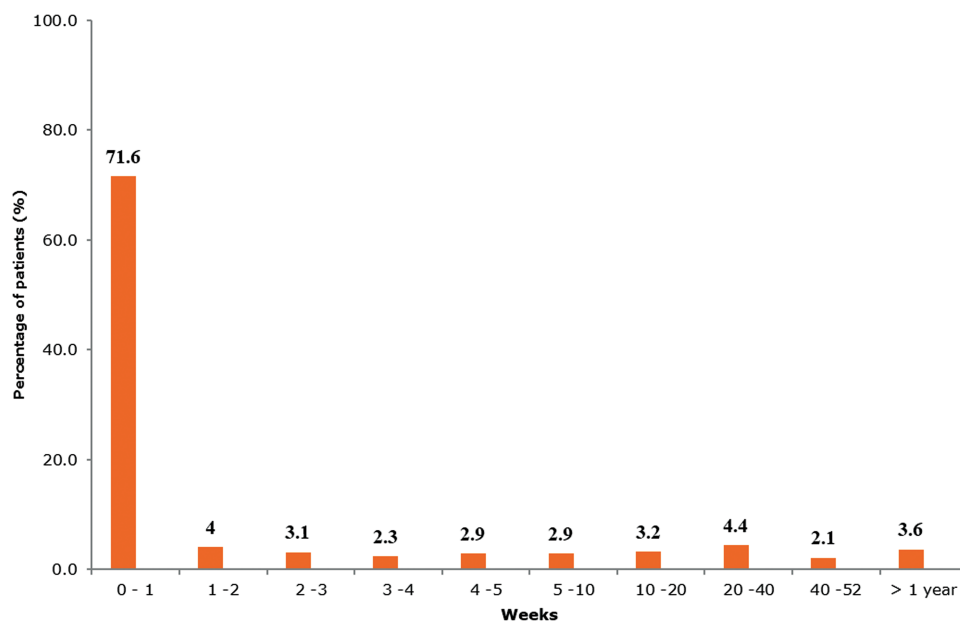
Adherence is defined as 80% PDC and greater during the whole follow-up duration.

ACEI/ARB = angiotensin-converting-enzyme inhibitor/angiotensin receptor blocker; CV = cardiovascular; CABG = coronary artery bypass graft surgery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation; TIA = transient ischemic attack; TIMI = thrombolysis in myocardial infarction; TRI = TIMI risk index.

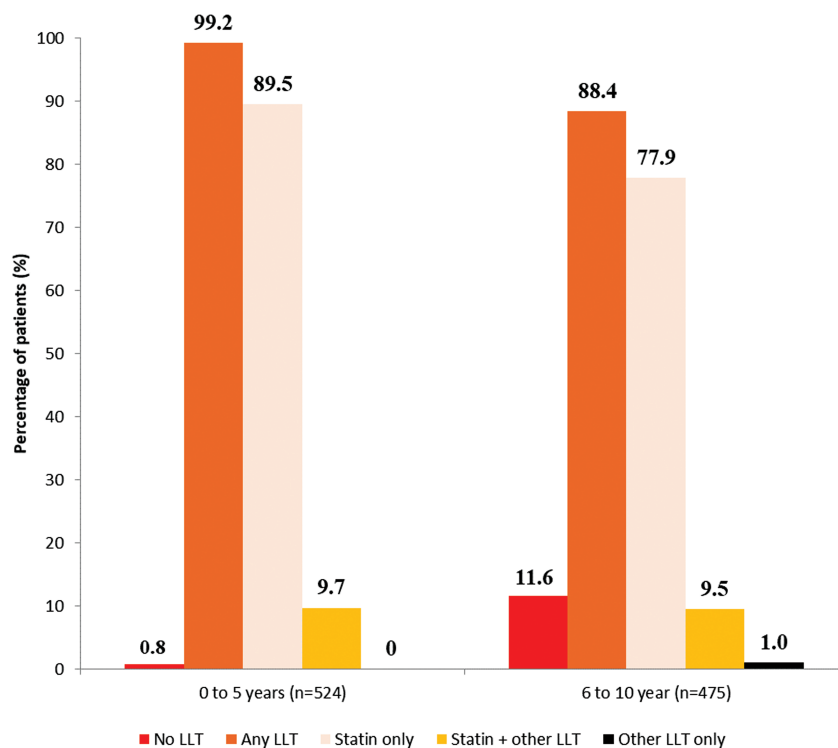
During the first year, 81% of patients were optimally adherent to statins; this percentage increased over the 10-year follow-up and reached 87% during the last year of follow-up (Figure 5). The percentages of patients with low statin adherence (21%-60%) and very low

statin adherence (<20%) remained stable at <12% during most of the study period, with the lowest at 8% during the last year. We observed a U-shape relationship between age and PDC with the highest PDC in patients aged between 60 and 80 years old (Figure 6).

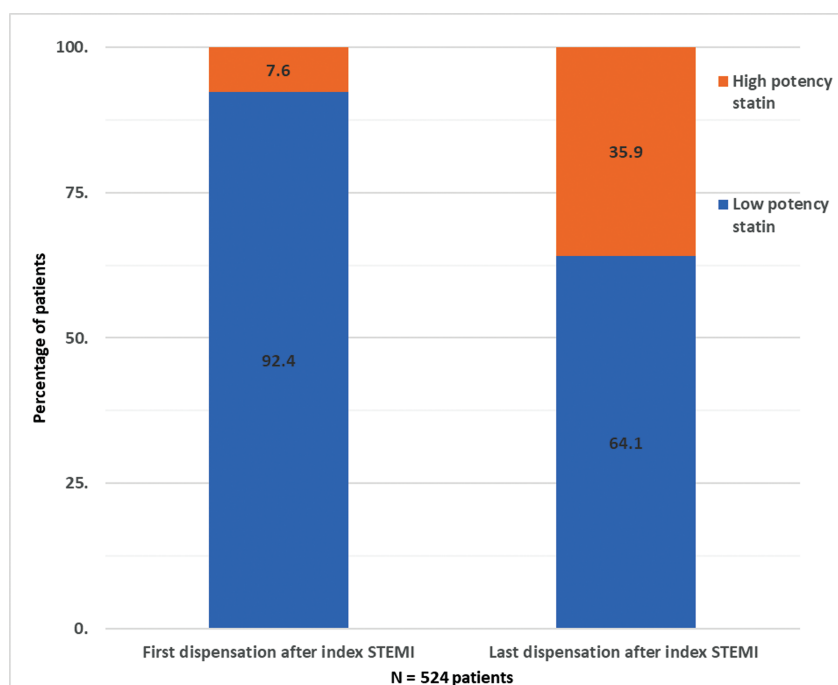
**FIG. 2** Days from hospital discharge to first dispensation of statin.



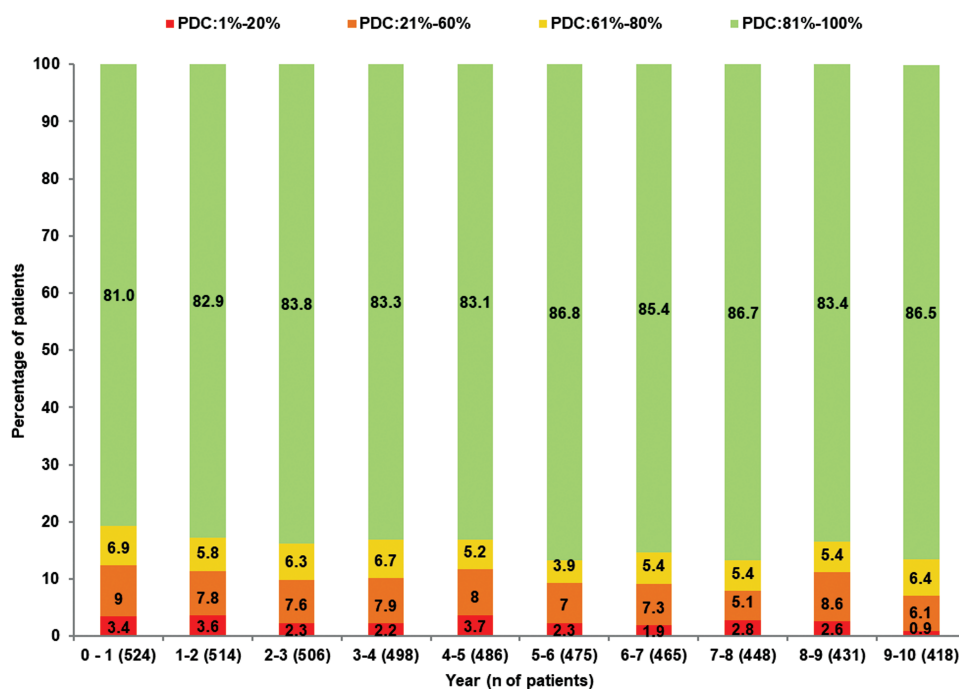
**FIG. 3** Types of lipid lowering therapies used during the 10-year follow-up.



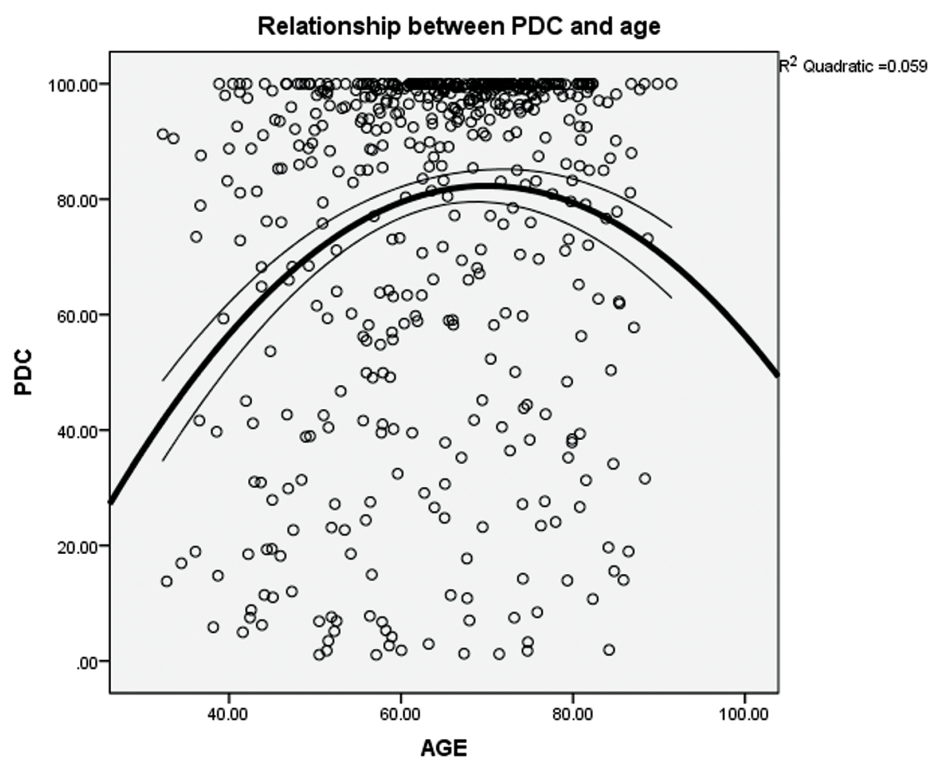
**FIG. 4** Dispensation of statins, stratified by potency and the first and last dispensation.



**FIG. 5** Adherence to statin by year.



**FIG. 6** Relationship between proportion of days covered and age.



We showed the independent predictors of optimal adherence in Table 2. Older age (up to the age of 80), living in areas within the two least socially deprived areas (Q1 and Q2), admission to a PCI-hospital and concomitant use of ACEI or ARB at hospital discharge were associated with increases in odds of optimal adherence. Living in the least

socially deprived areas Q1 and Q2 were associated with two and three-fold increases in odds of optimal adherence, respectively. Being prescribed ACEI or ARB at hospital discharge and admission to a PCI-hospital were associated with two-fold and 1.8-fold increases in odds of optimal adherence, respectively.

**TABLE 2** Determinants of Optimal Adherence

Predictors	Odds Ratio	95% Confidence Intervals		P-value
Age	1.02	1.004	1.04	0.02
Social deprivation, quintile 1*	1.86	1.009	3.43	0.05
Social deprivation, quintile 2*	2.99	1.60	5.59	0.0006
Social deprivation, quintile 3*	1.42	0.81	2.48	0.23
Social deprivation, quintile 4*	1.49	0.86	2.58	0.16
PCI-hospital	1.79	1.19	2.68	0.005
Use of ACE inhibitor and/or ARB at discharge	2.05	1.33	3.17	0.001

\*Compared to social deprivation quintile 5 (most deprived)

ACEI = angiotensin-converting-enzyme inhibitor; ARB = angiotensin receptor blockers; PCI = percutaneous coronary intervention.



## DISCUSSION

Our study provided insights into statin adherence over a long time horizon of 10 years. We showed that despite low or no-cost for drug dispensation, 12% of STEMI survivors remained non-optimally adherent to statin. Although the majority of patients (60%) filled their statin prescription within the first month of discharge, there remained a minority of patients (10%) who were dispensed statins much later (5 months or more). During the last 5 years, 12% of patients did not use any LLT. Older age, living in less socially deprived areas, concomitant use of ACEI/ARB, admission to PCI-hospitals were associated with improved statin adherence.

The stable rate of optimal adherence of our patients which remained at 80% and more during the 10-year follow-up was a definite improvement compared to previously reported adherence rates at 1-year and 5-year of 80% and 50%, respectively.<sup>3,8,13</sup> However, we noted three areas of sub-optimal LLT use: (1) lack of any LLT use in 12% of patients during the last 5 years, (2) although there was a temporal increase in use of high-potency statins, these medications remained under-used despite the well demonstrated benefits of high-potency statins<sup>25,26</sup> and (3) late statin refill (more than 5 months) in 10% of the STEMI survivors. Considering our low or no-cost statin dispensation and the risk of recurrent ischemia, adherence to LLT should be close to 100% in our cohort and patients unable to receive high-potency statins or any statin at all should have received alternate LLT either in single therapy or combined with statins.<sup>27,28</sup> Furthermore, all patients should have received expedient statin dispensation and use of high-potency statins should have been more emphasized.

Our analysis sheds some valuable insights into the independent determinants of long-term statin adherence within a system of care with low/no-cost statin dispensation. Age had variable influence on adherence within previous similar contexts with free or low-cost statin dispensation.<sup>3,21,22,29,30</sup> While Tuppin et al. reported worse adherence in the elderly,<sup>29</sup> others observed better adherence with advanced age.<sup>3,30</sup> Similar to Mann et al., we observed a U-shape relationship with patients aged from 60 to 80 years old having the most optimal adherence.<sup>30</sup> Our results

suggest that even with free or low-cost statin dispensation, other factors may confound the impact of age on statin adherence.

Patients with concomitant use of ACEI or ARB were more likely to be adherent to statins in our study. Use of ACEI or ARB may simply be a marker of better general adherence to therapies. Alternatively, concomitant use of ACEI or ARB may be a marker of sicker patients with more depressed cardiac function. Another potential hypothesis would be that concomitant use of ACEI or ARB may decrease side-effects to statins, hence improving long-term adherence to statins. Angiotensin II has been shown to increase oxidation of LDL.<sup>31</sup> It is therefore possible that by its anti-inflammatory action, angiotensin-renin blockade may have a direct benefit in decreasing inflammatory myopathy/myalgia in patients prone to statin intolerance. This hypothesis may be worth further exploration in larger studies.

Although PCI during the index STEMI hospitalization was not significantly associated with improved adherence, patients admitted at hospitals with an on-site PCI facility were twice more likely to be adherent compared to patients admitted at hospitals without on-site PCI facility. We are not aware of any evaluation of type of hospital on long-term statin adherence in STEMI survivors. Hospitals with on-site PCI facility are generally teaching hospitals with larger annual volumes of patients with STEMI. The impact of hospital's teaching status was variable in survivors of MI<sup>32,33</sup> with lower mortality in patients admitted at teaching hospitals<sup>32</sup> and neutral in other study.<sup>33</sup> It was possible, that in addition to the PCI facility, these institutions may offer better services to enhance support of STEMI survivors (such as cardiac rehabilitation or availability of lipidologists). Thereby, statin adherence may be improved in STEMI survivors by these aspects of care.

Little is known on the impact of social deprivation on long-term adherence to statins. Socially deprived areas in our study were areas with the most individuals who were either single, divorced, widowed, living alone or from a single-parent family. Socially deprived patients may not have the social support and encouragement which may improve long-term adherence to statin. Although the impact of social network was not consistently associated with medication adherence,

many of these studies were completed in patients with non-CV diseases (mainly immunodeficiency diseases).<sup>34</sup> It is therefore possible that social deprivation has more prominent impact on statin adherence than on adherence to other medications. In contrast to previous authors.<sup>16,17, 19,21</sup> we did not observe any effect of material deprivation on adherence to statins. This may be due to our low/no-cost statin dispensation.

### LIMITATIONS

Our study had a few noteworthy limitations. First, we had to exclude 213 patients (19% of our cohort) due to non-availability of their 10-year health data. Compared to patients with available 10-year health data, the excluded patients were older with more high-risk features (Appendix 2). Exclusion of these patients may have over-estimated our measures of adherence. Second, due to the inclusion of only patients with provincial drug coverage, our patients were particularly vulnerable individuals; such as elderly ( $\geq 65$  years old) and/or individuals with low income. Our findings therefore may not be entirely generalizable to younger patients and those with private drug insurance. Nevertheless, it remains highly likely that some of our observations such as the association of social deprivation with decreased adherence may be able to be replicated in different populations of patients. Third, we did not capture data on side-effects to statins, reasons for statin discontinuation and lipid profiles. This information would have been useful for our understanding of obstacles to statin adherence or low use of high-potency statins. Finally, the INSPQ evaluation of social deprivation was based mainly on the residential areas of the patients. Consequently, this assessment was subject to potential ecological bias whereby unknown confounders other than social deprivation may have modified statin adherence.

Compared to most prior studies of adherence, the strength of our analysis is based on complete statin refills information adjusted for hospitalization stays (when patients would not be able to take prescribed medications). Finally, the length of our follow-up exceeded most prior cohort studies on statin adherence.<sup>2,3,8,16-18,21,22,29</sup>

### CONCLUSIONS

Despite the low/no-cost medication dispensation, a minority of STEMI survivors were not using any type of LLT including statins during the long-term follow-up. Older age (up to 80 years), living in less socially deprived areas, concomitant use of ACEI or ARB, and admission to PCI-hospitals were associated with improved statin adherence. Future studies are needed to explore the potential factors associated with concomitant use of ACEI/ARB, and admission to PCI-hospitals that may have optimized statin adherence. Finally, socially deprived patients (single, widow, single-parent family member and those who lived alone) may benefit from more support and encouragement to enhance their long-term statin adherence.

### ACKNOWLEDGEMENT

The authors wish to acknowledge Mrs Marilyn de Chantal and Mrs Karine Alloul for their collaboration and support. The study was supported by Sanofi Canada.

### DISCLOSURE

Dr Thao Huynh received significant research supports from Sanofi Canada and Amgen Canada. The other authors did not have any significant conflict to disclosure.

### ROLE OF AUTHORS

Dr Thao Huynh is responsible for integrity of the data, was responsible for design and methodology; supervised project and wrote the final draft. All other co-authors reviewed and participated in the writing of the final manuscript.

### REFERENCES

1. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial Investigators. *N Engl J Med* 1996;335:1001-9.
2. Lemstra M, Blackburn DF. Nonadherence to statin therapy: Discontinuation after a single fill. *Can J Cardiol* 2012;28:567-73.

3. Blackburn DF, Dobson RT, Blackburn JL et al. Adherence to statins, beta-blockers and angiotensin-converting enzyme inhibitors following a first cardiovascular event: a retrospective cohort study. *Can J Cardiol* 2005;21:485–8.
4. Wong ND, Wong ND, Young D, et al. Prevalence of the American College of Cardiology/American Heart Association statin eligibility groups, statin use, and low-density lipoprotein cholesterol control in US adults using the National Health and Nutrition Examination Survey 2011–2012. *J Clin Lipidol* 2016;10:1109–18.
5. Lin I, Sung J, Sanchez RJ, et al. Patterns of statin use in a real-world population of patients at high cardiovascular risk. *J Manag Care Spec Pharm* 2016 Jun;22(6):685–98.
6. Steen DL, Khan I, Ansel D et al. Retrospective examination of lipid-lowering treatment patterns in a real-world high-risk cohort in the UK in 2014: comparison with the National Institute for Health and Care Excellence (NICE) 2014 lipid modification guidelines. *BMJ Open* Feb 2017;7(2): e013255.
7. Choudhry NK, Glynn RJ, Avorn J et al. Untangling the relationship between medication adherence and post-myocardial infarction outcomes: Medication adherence and clinical outcomes. *Am Heart J* 2014;167:51–8.
8. Ramsussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. *JAMA* 2007;297:177–86.
9. Blackburn DF, Dobson RT, Blackburn JL et al. Cardiovascular morbidity associated with nonadherence to statin therapy. *Pharmacotherapy* 2005;25:1035–43.
10. Pittman DG, Chen W, Bowlin SJ et al. Adherence to statins: subsequent healthcare costs and cardiovascular hospitalizations. *Am J Cardiol* 2011;107(11):1662–6.
11. Ho PM, Magid DJ, Shetterly SM et al. Medication non-adherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. *Am Heart J* 2008;155(4):772–9.
12. Aubert RE, Yao J, Xia F et al. Is there a relationship between early statin compliance and a reduction in healthcare utilization? *Am J Manag Care* 2010;16(6):459–66.
13. Ho PM, Bryson CL, Rumsfeld JS. Medication Adherence: Its Importance in cardiovascular outcomes. *Circulation* 2009;119:3028–35.
14. Karve S, Cleves MA, Helm M et al. Good and poor adherence: optimal cut-point for adherence measures using administrative claims data. *Curr Med Res Opin* 2009;25(9):2303–10.
15. Newby LK, LaPointe NM, Chen AY et al. Long-term adherence to evidence-based secondary prevention therapies in coronary artery disease. *Circulation* 2006 Jan17;113(2):203–12.
16. Perreault S, Blais L, Lamarre D et al. Persistence and determinants of statin therapy among middle-aged patients for primary and secondary prevention. *Br J Clin Pharmacol* 2005;59(5)564–73.
17. Lemstra M, Blackburn D, Crawley A, Fung R. Proportion and risk indicators of nonadherence to statin therapy: a meta-analysis. *Can J Cardiol* 2012;28:574–80.
18. Reuter H, Markhof A, Scholz S, et al. Long-term medication adherence in patients with ST-elevation myocardial infarction and primary percutaneous coronary intervention. *Eur J Prev Cardiol* 2015;22:890–8.
19. Avorn J, Monette J, Lacour A, et al. Persistence of use of lipid-lowering medications. a cross-national study. *JAMA* 1998;279(18):1458–62.
20. Desai NR and Choudhry NK. Impediments to adherence to post myocardial infarction medications. *Curr Cardiol Rep* 2013;15:322.
21. Chan DC, Shrank WH, Cutler D, et al. Patient, physician and payment predictors of statin adherence. *Med Care* 2010;48:196–202.
22. Régie de l'assurance médicament du Québec. Available at: <https://www.ramq.gouv.qc.ca>. Accessed on January 16, 2017.
23. Huynh T, O'Loughlin J, Joseph L et al. Delays to reperfusion therapy in acute ST-segment elevation myocardial infarction: results from the AMI-QUEBEC study. *CMAJ* 2006;175(12):1527–32.
24. Pampalon R, Gamache P, Hamel D. The Québec Index of Material and Social Deprivation Methodologic Follow-up, 1991 through 2006. Available at: [https://www.inspq.qc.ca/pdf/publications/1258\\_QcIndexDeprivation1991-2006.pdf](https://www.inspq.qc.ca/pdf/publications/1258_QcIndexDeprivation1991-2006.pdf).
25. LaRosa JC, Grundy SM, Waters DD, et al. intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med* 2005;352:1425–35.
26. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;350:1495–4.

27. Smith SC, Allen J, Blair SN et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update. *Circulation* 2006;113:2363–72.
28. Anderson T, Grégoire J, Pearson GJ, et al. 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. *Can J Cardiol* 2016;32:1263–82.
29. Tuppin P, Neumann A, Danchin N, et al. Evidence-based pharmacotherapy after myocardial infarction in France: adherence-associated factors and relationship with 30-month mortality and rehospitalization. *Arch Cardiovasc Dis* 2010;103(6-7):363–75.
30. Mann D, Woodard M, Muntner P, Falzon L, Kronish I. Predictors of non-adherence to statins: A systematic review and meta-analysis. *Ann Pharmacother* 2010;44(9):1410–21.
31. Nickenig G, Harrison DG. The AT1-Type angiotensin receptor in oxidative stress and atherogenesis. *Circulation* 2002;105:393–6.
32. Navathe AS, Silber JH, Zhu J, Volpp KG. Does admission to a teaching hospital affect acute myocardial infarction survival? *Acad Med* 2013;88:475–82.
33. Polanczyk CA, Lane A, Coburn M, et al. Hospital outcomes in major teaching, minor teaching, and nonteaching hospitals in New York State. *Am J Med* 2002;112:255–61.
34. Scheurer D, Choudhry N, Swanton KA, Matlin O, Shrank W. Association between different types of social support and medication adherence. *Am J Manag Care* 2012;18:e461–7.

## APPENDICES

### Appendix 1 List of Participating Hospitals

- |   |                                   |
|---|-----------------------------------|
| 1. Montreal General Hospital                        | 10. Hôpital général du Lakeshore  |
| 2. Hôpital général Juif                             | 11. Cité de la santé de Laval     |
| 3. Centre Hospitalier Chicoutimi                    | 12. Hôpital du Sacré-Coeur        |
| 4. Hôpital Sainte-Croix de Drummondville            | 13. Centre Hospitalier Notre Dame |
| 5. Institut de Cardiologie de Pneumologie de Quebec | 14. Royal Victoria Hospital       |
| 6. Centre hospitalier universitaire de Sherbrooke   | 15. Hôpital Ste Hyacinthe Yamaska |
| 7. Centre hospitalier régional de Lanaudière        | 16. Lasalle Hospital              |
| 8. Centre hospitalier de l'Amiante                  | 17. St-Mary Hospital              |
| 9. Centre hospitalier régional de l'Outaouais       |                                   |

### Appendix 2 Definition of Variables of Interest

Variables	Definition
Age	Age at the admission date of the index STEMI
Female	Sex at the admission date of the index STEMI
Diabetes mellitus	As captured in the hospital chart of the index STEMI
Beneficiaries of guaranteed income supplement	As captured in the provincial medication coverage dataset at the time of the index STEMI: low or no-income subjects who benefit from provincial/national income supplement and who also benefit from entirely free medication coverage (no co-pay).
Material deprivation	As determined by the INSPQ index in the provincial medication coverage dataset at the time of the index STEMI.
Social deprivation	As determined by the INSPQ index in the provincial medication coverage dataset at the time of the index STEMI.
Renal failure	During hospitalization of the index STEMI
GRACE score	As captured at initial presentation in the hospital chart of the index STEMI
LVEF	As captured at initial presentation in the hospital chart of the index STEMI
TIMI score	As captured at initial presentation in the hospital chart of the index STEMI
TRI index	As captured at initial presentation in the hospital chart of the index STEMI
Previous CV event	As captured in the hospital chart of the index STEMI: either previous known coronary artery disease/event/intervention, cerebral disease/event/intervention or peripheral artery disease/event/intervention.
Previous MI	As captured in the hospital chart of the index STEMI
Previous stroke	As captured in the hospital chart of the index STEMI

**Appendix 2** Definition of Variables of Interest (*Continued*)

<b>Variables</b>	<b>Definition</b>
Previous angioplasty	As captured in the hospital chart of the index STEMI
Previous bypass	As captured in the hospital chart of the index STEMI
Previous TIA	As captured in the hospital chart of the index STEMI
Anterior MI	Of the index STEMI
Killip class >1	As captured in the hospital chart of the index STEMI
Type of reperfusion therapy	As captured in the hospital chart of the index STEMI as the first treatment for the index STEMI
PCI hospital	As captured during the hospitalization of the index STEMI
PCI in hospital	On-site availability of cardiac catheterization laboratory able to perform PCI.
Major adverse events in hospital	As captured in the hospital chart of the index STEMI
Major bleed	As captured in the hospital chart of the index STEMI and as defined by the TIMI bleeding score
Heart failure	As captured in the hospital chart of the index STEMI (heart failure on physical exam and/or chest x-ray)
Reinfarction	As captured in the hospital chart of the index STEMI: re-elevation of cardiac biomarkers
In-hospital stroke	As captured in the hospital chart of the index STEMI
Discharge prescription	As captured in the hospital chart of the index STEMI, as noted in the exit prescription given to the patient at hospital discharge

*LVEF = left ventricular ejection fraction. MI = myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation; TIA = transient ischemic attack; TIMI = thrombolysis in myocardial infarction; TRI = TIMI risk index.*

**Appendix 3** Baseline Characteristics of All Patients: With and Without Available 10-Year Data

	<b>All patients N=1,071 (%)</b>	<b>10-year data available N=858 (%)</b>	<b>10-year data non available N=213 (%)</b>	<b>p-values*</b>
<b>Age, mean (SD)</b>	61.7 (12.9)	61.0 (12.8)	64.5 (12.9)	0.0003
<b>Female</b>	291 (27.2)	230 (26.8)	61 (28.6)	0.59
<b>Diabetes mellitus</b>	153 (14.3)	111 (12.9)	42 (19.7)	0.01
<b>Renal failure</b>	47 (4.4)	36 (4.2)	11 (5.2)	0.48
<b>Previous CV event</b>	219 (20.5)	170 (19.8)	49 (23.0)	0.30
<b>Previous MI</b>	144 (13.5)	111 (12.9)	33 (15.5)	0.33

**Appendix 3** Baseline Characteristics of All Patients: With and Without Available 10-Year Data (*Continued*)

	All patients N=1,071 (%)	10-year data available N=858 (%)	10-year data non available N=213 (%)	p-values*
Previous stroke	34 (3.2)	25 (2.9)	9 (4.2)	0.33
Previous angioplasty	112 (10.5)	88 (10.3)	24 (11.3)	0.67
Previous coronary artery bypass	39 (3.6)	31 (3.6)	8 (3.8)	0.92
Previous TIA	15 (1.4)	12 (1.4)	3 (1.4)	0.99
Anterior MI	503 (47.0)	395 (46.0)	108 (50.7)	0.22
Killip class >1	157 (14.66)	113 (13.17)	44 (20.66)	0.005
Type of reperfusion therapy				0.002
Fibrinolyse	407 (38)	337 (39.28)	70 (32.86)	
None	99 (9.24)	64 (7.46)	35 (16.43)	
Primary PCI	565 (52.75)	457 (53.26)	108 (50.7)	
PCI hospital	701 (65.45)	595 (69.35)	106 (49.77)	<0.0001
PCI in hospital	793 (74.04)	641 (74.71)	152 (71.36)	0.32
Major adverse events in hospital	151 (14.1)	105 (12.24)	46 (21.6)	0.0002
Major bleed	70 (6.54)	54 (6.29)	16 (7.51)	0.52
Heart failure	74 (6.91)	47 (5.48)	27 (12.68)	0.0002
Reinfarction	30 (2.8)	22 (2.56)	8 (3.76)	0.35
In-hospital stroke	8 (0.75)	4 (0.47)	4 (1.88)	0.03
Discharge prescription				
ACEI/ARB at hospital discharge	805 (75.16)	647 (75.41)	158 (74.18)	0.71
Aspirin	985 (91.97)	793 (92.42)	192 (90.14)	0.27
Aspirin and thienopyridine	769 (71.8)	631 (73.54)	138 (64.79)	0.01
Beta-blocker	907 (84.69)	732 (85.31)	175 (82.16)	0.25
Calcium channel blocker	65 (6.07)	43 (5.01)	22 (10.33)	0.004
Lipid-lowering therapy	855 (79.83)	697 (81.24)	158 (74.18)	0.02

\*Comparison between patients with and without 10-year survival data.

ACEI/ARB = angiotensin converting enzyme inhibitor/angiotensin receptor blocker; CV = cardiovascular; CABG = coronary artery bypass graft surgery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation; TIMI = thrombolysis in myocardial infarction.