Characterization of Statin Effectiveness Using Real-World Data in a Canadian Population

Sheri Shojaie[1], Sherri Thiele[1], Sean McCurdy[2], Lucy Ching Chau[3], Lindsay Martin[3], Katia Charland[1], Wendy N. Dobson-Belaire[1], Marc Duclos[1], Richard Borrelli[1]

[1] IMS Brogan, Mississauga, ON Canada L5N 6A4. [2] University of Toronto, Laboratory Medicine Pathology, Toronto, ON, Canada, M5S 1A1. [3] University of Toronto, Masters of Management of Innovation, Mississauga, ON, Canada, L5L 1C6

Objectives

Statins are widely used as a first-line treatment for hyperlipidemia and in the reduction of cardiovascular disease risk (CVD)[1]. As a result, statins are one of the most frequently prescribed classes of drugs in Canada, and constitute the leading drug cost in all provincial drug programs[2-4]. The Canadian Cardiovascular Society (CCS) recommends that physicians prescribe statins to patients largely based on their low density lipoprotein (LDL) levels and cardiovascular disease risk, determined by their Framingham risk score (FRS)[1]. Given the frequency of statin use and the considerable resources allocated to treatment, the aim of this study was to characterize the real world effect of statin therapy use on LDL levels and CVD risk during the first year of treatment.

Project Aims:

1. Characterize the demographic profiles of Canadian statin-treated patients within an electronic medical record database, IMS Brogan E360 EMR database
2. Describe the effect of statin treatment on patient LDL levels and change in CVD risk determined by the FRS within the first year of LDL initiation
3. Validate the use of FRS for determining CVD risk by comparing FRS to cardiovascular event-related ICD-9 diagnosis code frequency in patients

Methods

Data Source

Longitudinal patient-level records from an outpatient setting in Ontario, Canada were obtained from the IMS Brogan E360 EMR database (version 2015-04-24).

Study Design

Summary of the timelines associated with patient selection and study periods defining the analysis intervals are illustrated in **Figure 1.** This study is a follow-on to a cohort analysis presented at 2016 CADTH Symposium, Ottawa, Canada (April 10-12th)[5]. Final cohort of 1,046 patients meeting study inclusion/exclusion criteria (**Figure 2a**). A larger cohort of 5,006 patients was used in the diagnosis code analyses (**Figure 2b**). The list of molecules included in the study is shown in **Table 1**.

Framingham Risk Score

To evaluate the effect of statin therapy on cardiovascular risk, the Framingham Risk Score (FRS) was calculated to estimate the 10-year risk of experiencing an adverse cardiac event. Patient FRS prior to therapy initiation was compared to their FRS up to one year following statin therapy. The FRS is calculated based on a combination of demographic and recorded laboratory measures[6], summarized in **Figure 3**.

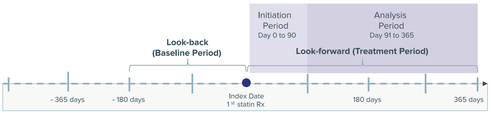


Figure 1. **Schematic of study period**

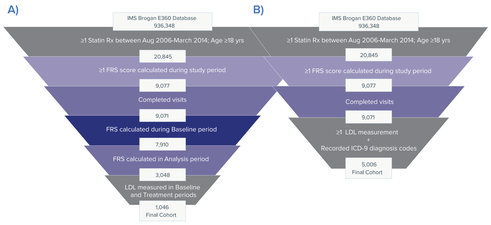


Figure 2. **A) Schematic of cohort selection criteria for statin treatment effectiveness analyses, B) Cohort selection criteria for diagnosis code frequency analyses**

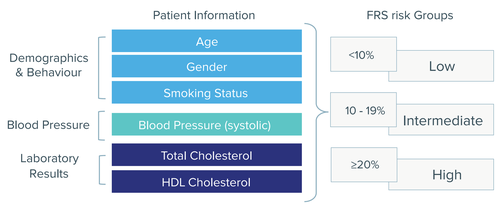


Figure 3. **Summary of variables used to calculate the Framingham Risk Score for determining the 10-year cardiovascular risk.**

Table 1. **List of statin and anti-hypertensive molecules included in the study**

Statin	atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatrin
Hypertensive	acebutolol, acetazolamide, aliskiren, amiloride, amlodipine, atenolol, benzapril, betaxolol, bisoproolol, bumetanide, captopril, chorthalidone, diltiazem, enalapril, ethacrynic acid, eprosartan, felodipine, fosinopril, furosemide, hydrochlorothiazide, inapamide, irbesartan, lisinopril, losartan, metolazone, metroprolol, nebivolol, nifedipine, nimodipine, perindopril

Results

Cohort baseline characteristics

- Demographic and recorded laboratory measures for patients in the study cohort (**Table 2**).

Effect of statin therapy on cholesterol levels

1. Statin therapy significantly decreases total cohort median LDL levels by 34% (3.5 to 2.3mmol/L, p<0.0001) and was similar across all FRS groups ranging from 32% to 37% reduction from baseline (**Figure 4**).
2. The proportion of patients that achieve LDL target was similar across FRS groups, though higher risk patients are more likely to reach target (statistically insignificant) (**Figure 5**).
3. Statin therapy significantly decreases cohort median total cholesterol levels by 20% (5.5 to 4.4mmol/L, p<0.0001), similarly across all FRS groups ranging from 17% to 23% reduction from baseline (**Figure 6**).

Table 2. **Cohort characteristics at baseline, prior to statin therapy initiation**

Variables	Total Cohort	Variables	Total Cohort
Cohort size, n	**1,046**	**LDL Cholesterol (mmol/L), median (Q1,Q3)**	**3.5 (2.6, 4.1)**
FRS, 10 year risk (Q1,Q3)	**4% (2%,10%)**	Less than 2, n (%)	119 (11.4%)
Age group, median (Q1,Q3)	**57 (49, 66)**	2 to 3.5, n (%)	440 (42.1%)
20 to 39, n (%)	66 (6.3%)	3.6 to 5, n (%)	416 (39.8%)
40 to 59, n (%)	534 (51.1%)	Greater than 5, n (%)	71 (6.8%)
60 to 95, n (%)	446 (42.6%)	**Total Cholesterol (mmol/L), median (Q1,Q3)**	**5.5 (4.6, 6.3)**
Sex, n (%)		<5.2, n (%)	446 (42.6%)
Male	541 (51.7%)	5.3-6.2, n (%)	297 (28.4%)
Female	505 (48.3%)	>6.2, n (%)	303 (29.0%)
Systolic pressure (mm Hg), median (Q1,Q3)	**134.5 (124,145)**	**FRS at Baseline, distribution, n (%)**	**1,046 (100%)**
Taking blood pressure medication, n (%)	**141 (13.5%)**	High	43 (4.1%)
Hypertensive (BP > 140/80), n (%)	**336 (32.1%)**	Intermediate	247 (23.6%)
		Low	756 (72.3%)

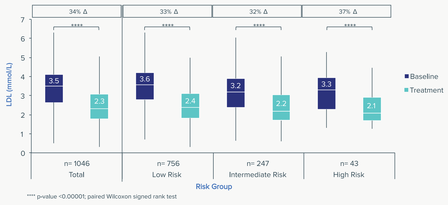


Figure 4. **LDL levels at baseline and treatment, stratified by baseline FRS risk group**

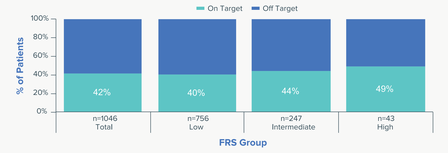


Figure 5. **Percent of patients that reach LDL target levels of 2mmol/L or a 50% reduction, stratified by baseline FRS risk group**

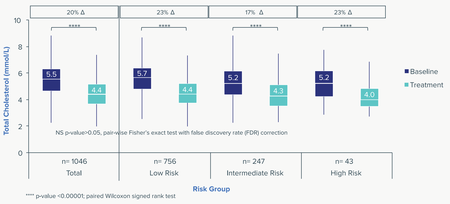


Figure 6. **Total cholesterol levels at baseline and treatment, stratified by baseline FRS risk group**

Effect of statin therapy on cardiovascular disease risk

4. Statin therapy significantly decreases FRS by 20% (5% to 4%, p<0.0001), similarly across all FRS groups. Statin-treatment did not change the patient's sub-cohort FRS risk group within one year of treatment (**Figure 7**).
5. High-risk group patients were two-times more likely to experience a cardiovascular event (relative risk 2.0, p<0.05) based on cardiovascular event-related diagnosis code frequency (**Figure 8**).

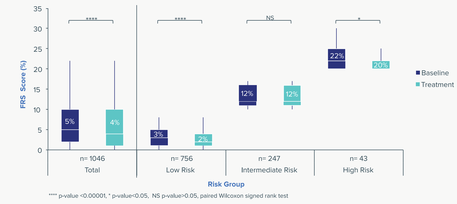
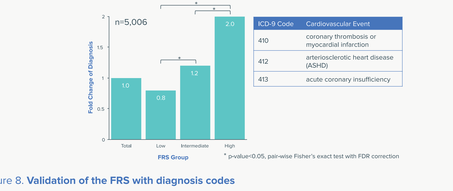


Figure 7. **Calculated FRS at baseline and treatment, stratified by baseline FRS risk group**



ICD-9 Code	Cardiovascular Event
410	coronary thrombosis or myocardial infarction
412	arteriosclerotic heart disease (ASHD)
413	acute coronary insufficiency

Figure 8. **Validation of the FRS with diagnosis codes**

Conclusions

Key findings:

- **Statin therapy initiation significantly reduces LDL levels and calculated FRS** within the first year of initiation
- Calculated **FRS is a valid measurement of cardiovascular disease risk**, based on reported CVD diagnosis code frequency
- Overall, **statin therapy had limited impact on the 10-year risk of adverse cardiovascular event occurrence during the first year of therapy**, as neither FRS sub-cohort dropped in risk group during the study period

Limitations

- 'High risk' patients may be underestimated during classification of FRS cohort as EMR data does not include current health state of patients such as prior stroke or bypass surgery
- Comorbidities and family history were not considered in the FRS calculation
- Diagnosis code may not be recorded at every patient visit, resulting in a potential gap in diagnosis recording
- Patient adherence and compliance to statin therapy was not evaluated and could impact observed outcomes

Future Directions

- Future work could examine the impact of longer treatment duration, specific statin molecules, dosages, or additional add-on treatment options for CVD risk management
- Additional analysis of comorbidities and family history could assist in aligning the EMR FRS calculations to real-world evidence
- Application of multi-dimensional predictive algorithms could find surrogate variables for family history and better identify 'high risk' patients
- Longer term study of statin effectiveness could better assess lasting impact on CVD risk

[1] *2012 Update of the Canadian Cardiovascular Society Guidelines for the Diagnosis and Treatment of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult.* **Todd J. AnderGrégoire J, Hegele R,Couture P, Mancini J, McPherson R, Francis G, Poirier P, Lau D, Grover S, Gen J**. 2, s.l. : Canadian Journal of Cardiology, 2013, Vol. 29.

[2] *Prescription medication use by Canadians aged 6 to 79.* **Rotermann, M, et al**. 6, 2014, Vol. 25, pp. 3-9.

[3] *The Canadian Rx Atlas.* **Morgan S, Smolina K, Mooney D et al**. Vancouver : Center for Health Services and Policy Research, 2013.

[4] *National Health Expenditure Trends, 1975 to 2003.* **Information, Canadian Institute for Health**. Ottawa : s.n., 2013, Canadian Institute for Health Information.

[5] *Comparing Guidelines for Statin Prescription Standards to Real-World Prescription Practices in Canada.* **Sherri Thiele, Sheri Shojaie, Sean McCurdy et al**. 2016 CADTH Symposium, Ottawa, Canada, 2016.

[6] *Prediction of coronary heart disease using risk factor categories.* **Wilson P, D'Agostino B, Levy D, Belanger A, Silbershatz H, Kannel W**. 18, s.l. : Circulation, 1998, Vol. 97.

imshealth™ | brogan