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Research Article

Is Treatment Inertia Unique to Publicly Funded Healthcare? Insights from the Guidelines Oriented Approach to Lipid lowering (GOAL) Canada Program

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Abstract

Background: We compared the use of lipid lowering therapy, low density-lipoprotein cholesterol (LDL-C) levels, and proportion achieving guideline-recommended LDL-C levels in patients with private vs. public insurance coverage for their lipid lowering treatment.

Materials and Methods: Guidelines Oriented Approach to Lipid lowering (GOAL) Canada enrolled 2009 patients with cardiovascular disease (CVD) or heterozygous familial hypercholesterolemia (FH) and an LDL-C above the guideline-recommended target of <2.0 mmol/L despite maximally tolerated statin therapy. During two follow-up visits physicians received online reminders of treatment recommendations.

Results: Of 2009 patients enrolled (median age 63 years, 42% female), there were 1284 (64%) patients with private and 725 (36%) with public insurance for lipid lowering therapy. Patients with private insurance were younger and less likely to have a history of heart failure or to be on bile acid sequestrants. There was no difference between the groups in their lipid levels or lipid lowering therapy at baseline. During the follow up, there was no difference in the use of ezetimibe; however, the use of PCSK9i was more frequent in patients with private insurance (31.7 % vs. 21%, p<0.0001), the mean LDL-C level was slightly lower (2.11±1.17 vs. 2.31±1.17 mmol/L, p = 0.001), and the proportion of patients achieving the guideline-recommended LDL-C level was greater (54% vs. 45.5%, p = 0.001). After adjustment for other factors in a multivariable model, private insurance was not a significant predictor of achieving the guideline-recommended LDL-C level in a multivariable model.

Conclusion: While PCSK9i use was higher in patients with private insurance, the majority of patients with either private or public insurance experienced similar treatment inertia. The cost of non-generic medications does not appear to be the dominant reason for the continued care gap in lipid lowering of high-risk patients.

Keywords: cardiovascular disease; familial hypercholesterolemia; Cardiovascular Medications

Introduction

Low-density lipoprotein cholesterol (LDL-C) level is a well-established risk factor for cardiovascular disease (CVD) and there is considerable evidence that lowering LDL-C reduces CVD morbidity and mortality. [1] Canadian Cardiovascular Society dyslipidemia guidelines [2] recommend initiation of LDL-C lowering with high intensity statin therapy with the addition of ezetimibe and / or PCSK9i as needed if LDL-C is not lowered by at least 50% or to the level below 2.0 mmol/L in patients with established CVD. Further, for those with a recent acute coronary syndrome and established coronary disease, consideration is to be given to more aggressive lowering of LDL-C to below 1.8 mmol/L. [2]

Nonetheless, strategies for lowering LDL-C are often poorly adopted in clinical practice, and many patients fail to reach guideline-recommended levels [4-8]. We have recently reported [9] that physician education based on a reminder approach imbedded into clinical practice, improves care significantly as measured by a higher proportion of patients achieving guideline-recommended LDL-C level in association with greater utilization of lipid lowering therapies.

This analysis explores whether patients with private insurance coverage and greater access for lipid lowering therapy experience achievement of recommended LDL-C level more frequently than those patients with public insurance only.

Materials and Methods

The Guidelines Oriented Approach to Lipid lowering (GOAL) Canada [9] was a medical education interventional program supported by Amgen Canada. It was an investigator-initiated study started in 2015 and coordinated by the Canadian Heart Research Centre, an academic research and physician education organization. The intervention studied was physician education based on lipid management reminders applied at the end of each of three visits based on data entry in an electronic case report form (eCRF) and the primary endpoint was proportion of patients achieving recommended LDL-C level of < 2.0 mmol/L in those with CVD and < 2.5 mmol/L or ≥ 50% reduction in those with heterozygous familial hypercholesterolemia (FH). All patients were recommended lifestyle modifications including dietary as recommended by the Canadian guidelines. [2] The study was approved by central and institutional research ethics boards where appropriate and all enrolled patients provided informed consent.

Invitations to participate were sent to a convenience sample of 750 Canadian physicians across Canada from a proprietary (CASL Regulation) Canadian Heart Research Centre list of physicians who participated in prior cholesterol-oriented data collection studies and 248 agreed to participate. The participating physicians had the primary and exclusive role in the management of their patients and selection of cholesterol lowering therapies. These physicians were asked to consecutively enrol at least 12 of their patients with either [1] clinical CVD including coronary artery disease (CAD), cerebrovascular disease, abdominal aortic aneurysm, or peripheral arterial disease; or, [2] FH. 2 Current use of PCK9i or prior participation in GOAL Program were the only exclusion criteria [9]. In addition, patient enrolment was allocated such that 2/3 of the patients were required to have private insurance and 1/3 public insurance only. All patients had to have [9] an LDL-C > 2.0 mmol/L despite maximally tolerated statin therapy (defined as having tried at least two statins, each at least on two reduced doses) for at least three months prior to enrolment. Lipid lowering treatment was assessed on enrolment (visit 1) and twice more during follow up, each approximately 4-6 months apart (visits 2 and 3). The medical education intervention consisted of physician reminders to follow Canadian guideline recommendations [2] at each visit; physicians were also asked to provide reason when guidelines were not followed.

Statistical Analysis

Continuous data are shown as means with standard deviation and categorical data as frequencies and percentages. Group comparisons were made using the chi squared test and t test or Kruskal-Wallis test for discrete and continuous variables, respectively, where appropriate. We used repeated measures analysis to perform univariate and multivariable regression to determine the outcome across the visits.

A multivariable logistic regression model was developed to assess factors independently associated with LDL-C achieving target (2) of ≤2.0 mmol. The following variables were considered: variables in Table 1 with p <0.05, type of insurance, use of statin, ezetimibe and PCSK9 inhibitor. To account for the clustering of patients within visits, we performed a generalized estimating equations (GEE) model. The working correlation structure selected was based on its lowest quasi-likelihood under the independence model criterion (QIC). Adjusted odds ratio (OR) with 95% confidence intervals (CI) are presented. A value of P<0.05 was considered significant for all tests except group comparison in Table 1 where correction for multiple (n = 31) comparisons was applied and value of P = 0.002 or less was considered significant. All statistical analyses were performed in SAS software version 9.4 (SAS Institute, Cary, NC).

Results

Of 2009 patients enrolled (median age 63 years, 42% female), there were 1284 (64%) patients with private insurance and 725 (36%) with public insurance only. Patients with private insurance were younger and less likely to have history of heart failure or to be on bile acid sequestrants (Table 1). There was no difference in LDL-C level between the two groups and no difference in the use of statin, including high intensity statin, or ezetimibe at baseline (Table 1).

Variables	Private (N=1284)	Public (N=725)	p
Age, years*	62±11	65±11	<.0001
Sex, female	519 (40%)	326 (45%)	0.05
Caucasian/White	921 (72%)	505 (70%)	0.33
Systolic Blood Pressure, mm Hg*	129±15	129±16	0.96
Diastolic Blood Pressure, mm Hg*	77±10	76±10	0.10
Heart rate, beat/minute*	72±11	73±11	0.67
Body Mass Index, kg/m^2*	29.8±7.0	29.1±6.1	0.02
Coronary artery disease	641 (50%)	395 (54%)	0.05
Cerebrovascular disease	103 (8%)	62 (9%)	0.68
Abdominal aortic aneurysm	23 (2%)	15 (2%)	0.66
Peripheral arterial disease	110 (9%)	73 (10%)	0.26
Microvascular disease	52 (4%)	36 (5%)	0.34
Familial hypercholesterolemia	614 (48%)	341 (47%)	0.74
Current or past history of smoking	600 (47%)	366 (50%)	0.11

Diabetes	448 (35%)	260 (36%)	0.66
Hypertension	751 (58%)	459 (63%)	0.03
Chronic kidney disease	99 (8%)	64 (9%)	0.38
Atrial fibrillation	78 (6%)	63 (9%)	0.03
Family history of premature CVD	557 (43%)	330 (46%)	0.35
Cancer	61 (5%)	37 (5%)	0.76
Heart failure	34 (3%)	39 (5%)	0.002
Liver disease	28 (2%)	13 (2%)	0.54
Aspirin	726 (57%)	427 (59%)	0.31
Other antiplatelet agent	201 (16%)	118 (16%)	0.71
ACE inhibitor	476 (37%)	291 (40%)	0.17
ARB	287 (22%)	163 (22%)	0.95
Beta blocker	488 (38%)	298 (41%)	0.17
Calcium Channel Blocker	279 (22%)	170 (23%)	0.37
Diuretic	223 (17%)	158 (22%)	0.02
Oral Anticoagulant	83 (6%)	62 (9%)	0.08
Spironolactone/Eplerenone	21 (2%)	13 (2%)	0.79
Total Cholesterol, mmol/L*	5.46±1.36	5.45±1.41	0.91
LDL-C, mmol/L*	3.34±1.27	3.34±1.27	1.00
HDL-C, mmol/L*	1.31±0.41	1.33±0.45	0.46
Non-HDL-C, mmol/L*	4.13±1.41	4.11±1.47	0.76
Triglycerides, mmol/L*	2.02±1.66	2.00±1.45	0.76
Statin	984 (77%)	551 (76%)	0.75
High intensity statin	551 (43%)	313 (43%)	0.91
Ezetimibe	332 (26%)	179 (25%)	0.56
High intensity statin + ezetimibe	144 (11%)	92 (13%)	0.32
Bile acid sequestrant	47 (4%)	55 (8%)	0.0001
Fibrate	41 (3%)	14 (2%)	0.10
Niacin	6 (0.5%)	2 (0.3%)	0.72

** Mean ± standard deviation*

Table 1: *Clinical Baseline Characteristics and Cardiovascular Medications*

During the follow up, the use of ezetimibe increased from approximately 25% at baseline to over 40% on visit 3 but remained similar between the two groups (Figure 1) while the use of PCSK9i was higher in patients with private insurance (31.7% vs. 21%, p=0.0001). The LDL-C level decreased slightly more in private insurance group at visit 2 (2.37±1.28 vs. 2.52±1.31, p=0.0165) and visit 3 (2.11±1.17 vs 2.31±1.17, p=0.0012). Proportion of patients achieving the recommended LDL-C level was 42.9% in private and 39.8% (p=0.2) in visit 2 and significantly greater in visit 3 (54.0% vs. 45.5%, p=0.001). Private insurance was not an independent predictor of achieving recommended LDL-C level in multivariable analysis (Table 2

Variables	Adjusted Odds Ratio (95% CI)	P value
Private vs Public insurance	1.01 (0.87-1.18)	0.88
Age (per year increase)	1.01 (1.01-1.02)	0.0005
BMI (per unit increase)	1.01 (1.00-1.02)	0.07
Female	0.62 (0.52-0.73)	<.0001
Coronary artery disease	1.47 (1.25-1.74)	<.0001
Hypertension	1.14 (0.96-1.35)	0.13
Atrial fibrillation	1.26 (0.95-1.67)	0.10
Heart failure	0.95 (0.63-1.42)	0.79
Diuretic	0.86 (0.70-1.05)	0.13
Statin	3.02 (2.48-3.69)	<.0001
Ezetimibe	1.66 (1.42-1.95)	<.0001
PCSK9 inhibitor	15.12 (12.07-18.96)	<.0001

Table 2: *Multivariable analysis to determine factors associated with achieving LDL-C ≤ 2.0 mmol/L (variables in the model are from Table 1 with p < 0.05 and lipid lowering agents*

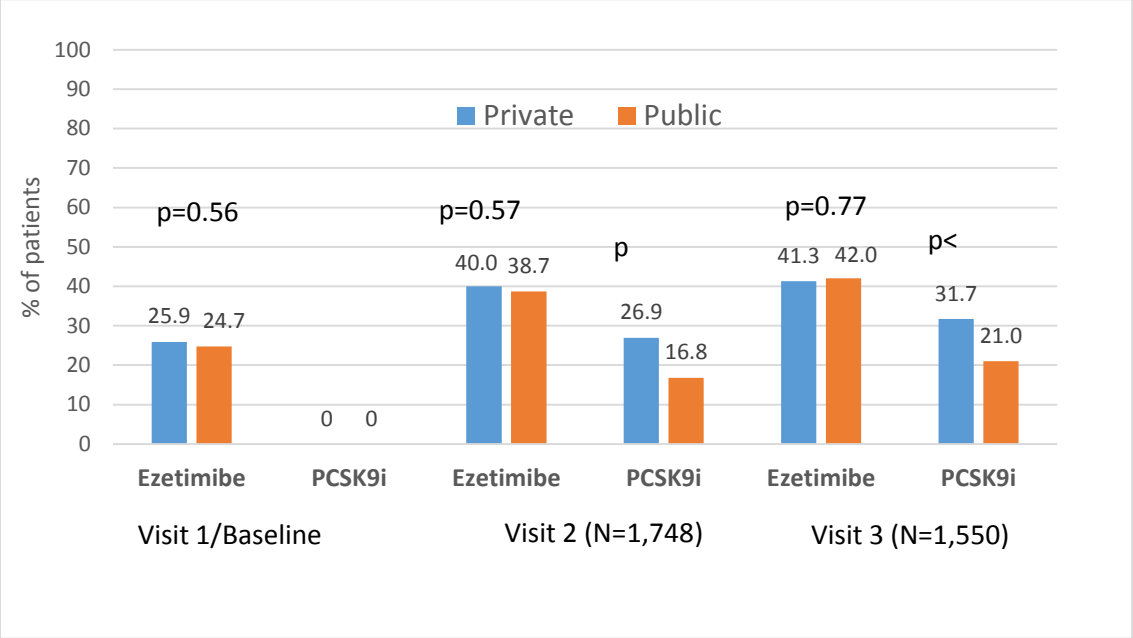

Figure 1: *Use of ezetimibe and PCSK9 inhibitor during follow up.*

Participating physicians were asked to provide the single most important reason for not being able to follow the guidelines for addition of non-statin therapy. It is notable that physicians identified cost as an issue for not prescribing more often in patients with public insurance as compared to private insurance for either ezetimibe (13.5% vs. 6.6%, p=0.0004) or PCSK9i (33.8% vs. 20.5%, p=0.0001).

Discussion

Established CVD and FH are both associated with major adverse cardiovascular morbidity and mortality. Despite the use of high intensity statin therapy, many patients do not achieve the recommended LDL-C level. [10-12] The addition of second and third-line non-statin therapies has been shown to further reduce CV events. [13-15]

We found that the availability of private insurance was associated with a 10% greater use of PCSK9i but had no impact on the use of genericized high intensity statin or ezetimibe or both. The greater use of PCSK9i was associated with achievement of the recommended LDL-C level as was the use of statin or ezetimibe therapy. However, availability of private insurance was not predictive of better LDL-C target achievement level in multivariable analysis.

The treatment inertia observed in these high-risk patients was more similar than different between the two groups with private and public only insurance, since most of these patients were not on either PCSK9i or ezetimibe by the end of the follow up.

Our prior observations demonstrate benefit of educational intervention on treatment inertia. [9,16,17] Our findings suggest that the availability of private insurance may play a role in achieving the recommended management in lipid lowering but the benefit of private insurance is modest and the cost of medications itself is not a factor in physicians' ability to follow the guideline recommended therapy. These findings are consistent with our prior observations on guidelines-oriented management of diabetes mellitus in Canada. [18] Accordingly, other factors may be important. For example, private insurance coverage may vary across Canada with respect to coverage of conditions such as FH. In addition, it is not uncommon for access with or without private insurance to require filling of multiple forms, sometimes multiple times, thereby leading to some inertia irrespective of private coverage. This may account for the improved but less than expected uptake of PCSK9 inhibitors in patients with private coverage. This and other barriers that impair achievement of an LDL-C treatment goal may require fuller exploration from both the perspective of patients as well as treating physicians.

Limitations

This post-hoc analysis is subject to physician and patient selection bias. Physicians invited to participate had prior experience in similar programs and therefore may not be representative of all Canadian health care providers. The extent of the care gap detected, and low use of statin and non-statin therapy argues against selection bias of physicians skilled in the LDL-C management.

While these selection biases may limit the generalizability of our findings, they in no way diminish the validity of our conclusions about the existence of the treatment inertia and only modest impact of private insurance in lipid lowering therapy.

Conclusion

While PCSK9i use was higher in patients with private insurance, the majority of patients with either private or public insurance experienced similar treatment inertia. The cost of medications does not appear to be the dominant reason for care gap in lipid lowering of higher risk patients.

DISCLOSURES:

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