Prevalence of dyslipidemia in statin-treated patients in Canada: Results of the DYSlipidemia International Study (DYSIS)

Shaun G Goodman MD MSc[1,2], Anatoly Langer MD MSc[1,2], Natacha R Bastien PhD[3], Ruth McPherson MD MSc PhD[4], Gordon A Francis MD[5], Jacques J Genest Jr MD[6], Lawrence A Leiter MD[1]; on behalf of the DYSIS Canadian Investigators*

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BACKGROUND: Despite clear guideline recommendations, there is a growing body of evidence that there is suboptimal use of lipid-lowering treatment in Canadians.
OBJECTIVE: To assess the prevalence and types of persistent lipid abnormalities in Canadian patients receiving statin therapy.
METHODS: The present cross-sectional study recruited 2436 outpatients 45 years of age or older who were treated with statins by 232 physicians from 10 provinces; all underwent clinical examination and had their latest fasting lipid values while on statin therapy recorded.
RESULTS: The median patient age was 66 years (interquartile range [IQR] 58 to 74 years), 60% were men and 80% were in the high 10-year risk category. The median low-density lipoprotein cholesterol level was 2.0 mmol/L (IQR 1.6 mmol/L to 2.5 mmol/L) and the median total cholesterol/high-density lipoprotein cholesterol ratio was 3.4 mmol/L (IQR 2.8 mmol/L to 4.1 mmol/L). However, based on the 2006 Canadian Cardiovascular Society recommendations, 37% of all patients did not have a low-density lipoprotein cholesterol level at goal or intervention target level, including 45% of high-risk category patients. The majority of patients received atorvastatin (50%) or rosuvastatin (37%) but primarily at low-to-medium doses, and a minority (14%) received additional lipid-modifying therapies.
CONCLUSIONS: The present observational study highlights the need for more intensive treatment of lipid abnormalities, particularly among high-risk patients. Recognizing several important limitations related to the observational nature of the study, the findings suggest the possibility that, in addition to optimizing adherence, there remains an important need to titrate current statin therapy to higher doses and potentially use a combination of lipid-modifying treatments (once the statin dose has been truly maximized) to further bridge the gap between evidence-based medicine and current Canadian practice.

Key Words: *Cholesterol; Dyslipidemia; Lipids*

La prévalence de dyslipidémie chez des patients traités par statines au Canada : Les résultats de l'étude internationale sur la DYSlipidémie (DYSIS)

HISTORIQUE : Malgré des recommandations claires, de plus en plus de données probantes font foi d'une utilisation sous-optimale des hypolipidémiants chez les Canadiens.
OBJECTIF : Évaluer la prévalence et les types d'anomalies lipidiques persistantes chez les patients qui suivent une thérapie aux statines.
MÉTHODOLOGIE : Dans le cadre de la présente étude transversale, les chercheurs ont recruté 2 436 patients en consultations externes de 45 ans ou plus traités aux statines par 232 médecins de dix provinces. Tous ont subi un examen clinique et ont vu leurs valeurs lipidiques à jeun les plus récentes se faire consigner pendant qu'ils suivaient une thérapie aux statines.
RÉSULTATS : Les patients avaient un âge médian de 66 ans (plage interquartile [PIQ] de 58 à 74 ans), 60 % étaient des hommes et 80 % étaient dans la catégorie à haut risque sur dix ans. Leur taux médian de cholestérol à lipoprotéines de basse densité était de 2,0 mmol/L (PIQ de 1,6 mmol/L à 2,5 mmol/L) et le ratio médian entre le cholestérol total et le cholestérol à lipoprotéines de basse densité, de 3,4 mmol/L (PIQ de 2,8 mmol/L à 4,1 mmol/L). Cependant, d'après les recommandations de la Société canadienne de cardiologie de 2006, le taux de cholestérol à lipoprotéines de basse densité de 37 % de tous les patients ne correspondait pas à l'objectif ou aux cibles d'intervention, y compris 45 % des patients de la catégorie à haut risque. La majorité des patients ont reçu de l'atorvastatine (50 %) ou de la rosuvastatine (37 %), mais surtout à des doses basses à moyennes, et une minorité (14 %) ont reçu d'autres modificateurs des lipides.
CONCLUSIONS : La présente étude d'observation fait ressortir la nécessité de traiter plus intensivement les anomalies lipidiques, surtout chez les patients à haut risque. Compte tenu de plusieurs limites importantes liées à la nature observationnelle de l'étude, les observations indiquent la possibilité que, en plus d'optimiser l'adhésion, il est nécessaire de titrer la thérapie aux statines actuelles à des doses plus élevées et, peut-être, d'utiliser une association de modificateurs des lipides (une fois la dose de statines véritablement maximisée) pour mieux corriger l'écart entre la médecine probante et la pratique canadienne actuelle.

Epidemiological evidence supports a strong relationship between elevated levels of plasma cholesterol, particularly low-density lipoprotein cholesterol (LDL-C), and increased risk for cardiovascular disease. LDL-C lowering has been the primary goal of therapy aimed at cardiovascular risk reduction, and multiple randomized studies have demonstrated the benefits of statins for the reduction of major cardiovascular events in patients at risk (1). Consequently, lipid lowering with a statin has become a key recommendation to Canadian physicians who manage patients with cardiovascular disease or those at risk for cardiovascular disease (2).

Despite well-documented risk reductions associated with LDL-C lowering, a substantial number of clinical events are not prevented by statins, even when used with other evidence-based therapies (3). Furthermore, there is a growing body of evidence that, despite clear guideline recommendations (2), there is suboptimal utilization of lipid-lowering treatment in Canadians (4,5).

The objective of the current study was to assess the prevalence and types of persistent lipid abnormalities in Canadian patients receiving statin therapy, with the aim of establishing a framework within which recommendations for future treatment practice might be made.

[1]*St Michael's Hospital and University of Toronto;* [2]*Canadian Heart Research Centre, Toronto; Ontario;* [3]*Merck Frosst Canada Ltd, Kirkland, Quebec;* [4]*University of Ottawa Heart Institute, Ottawa, Ontario;* [5]*University of British Columbia, Vancouver, British Columbia;* [6]*McGill University, Montreal, Quebec*

**Participating Canadian DYSIS Registry Investigators are listed in the Appendix; LA Leiter served as the Canadian National Leader for DYSIS*

Correspondence: Dr Shaun G Goodman, Division of Cardiology, St Michael's Hospital, 30 Bond Street, Room 6-034, Toronto, Ontario M5B 1W8. Telephone 416-864-5722, fax 416-864-5407, e-mail goodmans@smh.toronto.on.ca

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METHODS

The DYSlipidemia International Study (DYSIS) (6) is an international epidemiological multicentre, cross-sectional study of the lipid profile of 22,063 statin-treated outpatients The current analysis includes only those patients enrolled in Canada. Patients were eligible for study inclusion if they were 45 years of age or older, had been on statin therapy for three or more months at the time of assessment, had at least one lipid parameter available based on a fasting profile obtained as part of routine clinical care within the previous six months, and provided written informed consent. The only exclusion criterion was active participation in a clinical study.

Physicians were recruited by direct mail or fax campaigns, continuing medical education events, and from participation in previous or ongoing registries of the coordinating centre – the Canadian Heart Research Centre (Toronto, Ontario). The study protocol was approved by independent central ethics review boards (Optimum Clinical Research Inc, Oshawa, Ontario; and the College of Physicians & Surgeons of Alberta Research Ethics Review Committee, Edmonton, Alberta). Participating physicians were instructed to enrol consecutive patients visiting their practice over a two-month period who met the inclusion criteria, irrespective of the clinical reason for the office visit.

Data were collected from clinical examination and medical charts during a single outpatient visit between April 2008 and February 2009, and submitted via a standardized case report form to the Canadian coordinating centre. Data were subsequently entered into a central electronic (web-based) database housed and managed at the Institut für Herzinfarktforschung Ludwigshafen an der Universität Heidelberg (Germany). Real-time quality control (internal logic checks) occurred during web-based data entry.

Patient demographic and clinical data, and information on treating physicians (including their speciality, medical practice and location) were collected. Lipid parameters from the most recent lipid test available within the previous six to 12 months (based on local testing frequency) for total cholesterol (TC), LDL-C, high-density lipoprotein cholesterol (HDL-C), TC/HDL-C ratio and triglycerides were recorded. Specific patient-related lipid targets, whether patients were at goal levels, and the relevance of the different lipid parameters for the physicians were also recorded. The 2006 Canadian Cardiovascular Society recommendations were used to classify patient risk, and define the LDL-C and TC/HDL-C goals and intervention targets (2).

Information collected on lipid therapies included the name and daily dose of the current statin, and whether the primary reason for use was hypercholesterolemia, as well as the name and daily dose of the statin in use at the time of the most recent blood test. Other cardiovascular therapies taken by the patient were also recorded.

Categorical variables are presented as absolute numbers and percentages. Continuous variables are summarized as medians with 25th and 75th percentiles (interquartile range [IQR]). Multivariable logistic regression analysis was performed to determine the factors in high-risk patients associated with LDL-C values and TC/HDL-C ratios not at goal (less than 2.0 mmol/L and less than 4, respectively) (2). Based on the results of previous studies (4,7), the predictor variables considered in the models were age, sex, current smoker, sedentary lifestyle (physical activity less than the equivalent of walking 20 min to 30 min, three to four days a week), body mass index 30 kg/m^2 or greater, waist circumference greater than 102 cm in men and greater than 88 cm in women, hypertension, diabetes mellitus, history of ischemic heart disease, cerebrovascular disease and peripheral artery disease. Adjusted ORs with 95% CIs were calculated. All analyses were performed using SAS version 9.1 (SAS Institute Inc, USA). All statistical comparisons were two-tailed, and $P<0.05$ was considered to be statistically significant.

RESULTS

Data from 2436 consecutive statin-treated outpatients of 232 Canadian physicians (84.5% primary care physicians and 15.5% specialists) from 10 provinces were analyzed. Patient characteristics, risk categories and lipid values are reported in Table 1. The median patient age was 66 years (IQR 58 to 74 years) and the majority were men (59.8%); 50.8% met the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria for the metabolic syndrome (8) and 44.7% were obese. Comorbidities were common, including hypertension (75.2%), diabetes mellitus (47.8%) and previous cardiovascular disease (ischemic heart disease, heart failure, peripheral arterial disease or cerebrovascular disease [44.8%]). The majority (80%) of patients fell into the high 10-year risk category (cardiovascular disease, diabetes mellitus or a Framingham risk score of 20% or greater) (2).

The median LDL-C was 2.0 mmol/L (IQR 1.6 mmol/L to 2.5 mmol/L) and the median TC/HDL-C ratio was 3.4 (IQR 2.8 to 4.1). The lipid profile stratified according to Canadian Cardiovascular Society cardiovascular risk category is provided in Table 2. Of note, 37% of all patients did not have an LDL-C at goal (defined as 2.0 mmol/L or greater for high risk) or intervention levels (3.5 mmol/L or greater for intermediate risk, and 5.0 mmol/L or greater for low risk [2]), including 45% of high-risk category patients. Overall, 23.3% of patients had a TC/HDL-C ratio above the guideline-recommended goal (high risk 4 or greater) or intervention levels (intermediate risk 5 or greater, and low risk 6 or greater), including 27.5% of high-risk patients. Atorvastatin was the most frequently prescribed statin (49.7%) followed by rosuvastatin (37.4%), simvastatin (9.5%), pravastatin (2.5%), lovastatin (0.7%) and fluvastatin (0.2%). Only 14.2% of patients received additional lipid-modifying therapies: ezetimibe (11.1%), fibrate (2.3%), nicotinic acid (1.3%) and bile acid sequestrant (0.4%). The median daily dose of the most commonly used statins at the time closest to the most recent lipid profile was atorvastatin 20 mg (IQR 10 mg to 40 mg), rosuvastatin 10 mg (IQR 10 mg to 20 mg) and simvastatin 40 mg (IQR 20 mg to 40 mg).

In Table 3, lipid profiles are stratified according to a history of diabetes and/or cardiovascular disease. The LDL-C and TC/HDL-C goals were not achieved in 40% and 27.3% of patients with diabetes, and 44.6% and 26.4% of patients with cardiovascular disease, respectively.

In multivariable logistic regression analysis, several demographic and clinical features were independently associated with lack of achievement of target LDL-C (ie, greater than 2.0 mmol/L), and both target LDL-C and TC/HDL-C ratio (ie, greater than 4) among high-risk patients (n=1945; 80% of the overall population) (Tables 4 and 5). Female sex was an independent predictor of an LDL-C greater than 2.0 mmol/L, and a sedentary lifestyle (but not female sex) was an independent predictor of both an LDL-C greater than 2.0 mmol/L and a TC/HDL-C ratio greater than 4. In contrast, patients of older age with diabetes and previous ischemic heart disease were less likely to have an LDL-C greater than 2.0 mmol/L and a TC/HDL-C ratio greater than 4. Body mass index, waist circumference, hypertension, cerebrovascular disease and peripheral arterial disease were not related to target values. Of note, physician specialty (eg, cardiologist, endocrinologist, internal medicine specialist versus general practitioner/family physician) was not an independent predictor in additional models evaluating lack of achievement of target levels.

DISCUSSION

The results of the present observational study suggest that almost one-half of the high-risk Canadian patients with cardiovascular disease, diabetes or an estimated 10-year coronary artery disease risk of 20% or greater did not reach the LDL-C target recommended by Canadian guidelines (2). These contemporary findings are supported by other recently published Canadian reports (4,5) including a study (9) that used a flexible starting dose of a statin to quickly achieve an LDL-C target.

Several reasons may account for the suboptimal rate of adherence to Canadian treatment guidelines. While lack of awareness of treatment guidelines (ie, a knowledge gap attributed to physicians) could

TABLE 1
Patient characteristics, risk categories and lipid parameters

	All patients	Men	Women
n (%)	2436*	1457 (59.8)	979 (40.2)
Age, years	66 (58–74)	65 (58–73)	67 (59–74)
Caucasian, %	86.1	87.0	84.7
Family history of premature coronary disease†, %	34.3	32.0	37.8
Ischemic heart disease, %	37.3	45.7	24.7
Peripheral arterial disease, %	8.5	9.2	7.5
Cerebrovascular disease, %	8.5	8.5	8.6
Heart failure, %	4.6	5.0	3.9
Current smoker, %	14.1	13.9	14.4
Hypertension, %	75.2	73.1	78.2
Systolic blood pressure, mmHg	130 (120–137)	128 (120–136)	130 (120–138)
Diastolic blood pressure, mmHg	76 (70–80)	76 (70–80)	76 (70–80)
Waist circumference, cm	101 (92–111)	104 (95–113)	96 (86–107)
Body mass index, kg/m^2	29.2 (25.9–33.5)	29.4 (26.3–33.5)	28.8 (25.3–33.6)
Body mass index ≥30 kg/m^2, %	44.7	45.6	43.4
The metabolic syndrome‡, %	50.8	45.6	58.6
Risk level§, %			
High	80.0	85.8	71.4
Intermediate	8.1	8.8	7.0
Low	11.9	5.4	21.6
Cardiovascular disease¶, %	44.8	52.0	34.2
Diabetes mellitus, %	47.8	46.6	49.4
Hemoglobin A1c, %	6.8 (6.3–7.6)	6.9 (6.3–7.7)	6.7 (6.3–7.5)
Lipid profile			
LDL-C, mmol/L	2.0 (1.6–2.5)	2.0 (1.6–2.4)	2.2 (1.7–2.7)
HDL-C, mmol/L	1.1 (1.0–1.4)	1.1 (0.9–1.3)	1.3 (1.1–1.5)
TC, mmol/L	4.0 (3.4–4.6)	3.8 (3.3–4.4)	4.2 (3.7–4.9)
Triglycerides, mmol/L	1.4 (1.0–2.0)	1.4 (1.0–2.0)	1.5 (1.1–2.1)
TC/HDL-C ratio	3.4 (2.8–4.1)	3.5 (2.9–4.2)	3.3 (2.7–4.0)

*Data presented as median (interquartile range) unless otherwise indicated. *Missing values for race (n=15), hypertension (n=1), systolic blood pressure (n=1), diastolic blood pressure (n=1), waist circumference (n=11), metabolic syndrome determination (n=64), risk level determination (n=5), diabetes status (n=1), low-density lipoprotein cholesterol (LDL-C) (n=26), high-density lipoprotein cholesterol (HDL-C) (n=9), total cholesterol (TC) (n=11) and triglycerides (n=13); †First-degree relative (parents, brothers or sisters) suffered any early manifestation of atherosclerotic cardiovascular disease (younger than 55 years of age in men and younger than 65 years of age in women); ‡The metabolic syndrome is defined as abdominal obesity (waist circumference greater than 102 cm for men and greater than 88 cm for women), triglycerides 1.7 mmol/L, HDL-C greater than 1.03 mmol/L (men) or less than 1.29 mmol/L (women), blood pressure 130/85 mmHg or greater and fasting glucose 6.1 mmol/L or greater; §High risk: coronary artery disease, peripheral arterial disease, cerebrovascular disease, diabetes mellitus, or Framingham 10-year risk score 20% or greater. Intermediate risk: Framingham 10-year risk score 10% to 19%. Low risk: Framingham 10-year risk score less than 10%; ¶Ischemic heart disease, heart failure, peripheral arterial disease or cerebrovascular disease*

TABLE 2
Lipid abnormalities according to Canadian guideline risk levels (2) in patients with complete lipid profiles

	All patients (n=2393)	High risk* (n=1913)	Intermediate risk* (n=191)	Low risk* (n=289)
LDL-C not at goal/intervention target†	37.0	45.0	11.5	0.7
TC/HDL-C ratio not at goal/intervention target‡	23.3	27.5	13.6	1.4
LDL-C and TC/HDL-C ratio not at goal/intervention target	16.1	19.7	4.2	0.0
Elevated triglycerides§	36.9	37.7	31.4	35.3

*Data presented as %. *High-risk: coronary artery disease, peripheral arterial disease, cerebrovascular disease, diabetes mellitus or Framingham 10-year risk score 20% or greater. Intermediate risk: Framingham 10-year risk score 10% to 19%. Low-risk: Framingham 10-year risk score less than 10%; †Low-density lipoprotein cholesterol (LDL-C) 2.0 mmol/Lor greater in high-risk patients, 3.5 mmol/L or greater in intermediate-risk patients, and 5.0 mmol/L or greater in low-risk patients; ‡Total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C) ratio: high risk is 4 or greater, intermediate risk is 5 or greater, low risk is 6 or greater; §1.7 mmol/L or greater*

be considered, our previous experience suggests that this is not the main contributor. Indeed, in the Guidelines Oriented Approach to Lipid Lowering (GOALL) Registry chart review (6236 Canadian patients at intermediate to high risk and cared for by 335 primary care practitioners) and main study (4499 patients from 254 general practitioners) (4), physicians correctly identified the target lipid levels for the majority of patients overall (greater than 90%) and for high-risk patients (96%), respectively. Furthermore, we did not find that the type of physician (specialist versus general practitioner/family physician) was independently associated with achievement of target levels.

Our results suggest that there continue to be significant barriers to translating evidence-based, guideline-recommended targets into routine Canadian practice. These may include suboptimal drug or dose selection, failure to titrate therapy, patient adherence or limited efficacy (4). While 88% of all patients received one of the more 'potent' statins, the median daily doses of atorvastatin (20 mg) and rosuvastatin (10 mg) were lower than those used in clinical outcome

TABLE 3
Lipid abnormalities according to diagnosis of diabetes mellitus and/or cardiovascular disease (CVD)*

	All diabetes (n=1137)	Diabetes without CVD (n=711)	All CVD (n=1079)	CVD without diabetes (n=652)
LDL-C not at goal†	40.0	41.2	44.6	48.8
TC/HDL-C ratio not at goal‡	27.3	26.3	26.4	24.7
LDL-C and TC/HDL-C ratio not at goal	18.5	19.8	17.8	18.7
Elevated triglycerides§	40.0	39.2	36.5	33.4

*Data presented as %. *Ischemic heart disease, heart failure, peripheral arterial disease or cerebrovascular disease; †Low-density lipoprotein cholesterol (LDL-C) 2.0 mmol/L or greater in high risk patients, 3.5 mmol/L or greater in intermediate risk patients, and 5.0 mmol/L or greater in low-risk patients; ‡Total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C) ratio: high risk 4 or greater, intermediate risk 5 or greater, low risk 6 or greater; §1.7 mmol/L or greater*

TABLE 4
Multivariable analysis: Factors associated with lack of achievement of target low-density lipoprotein cholesterol (ie, greater than 2.0 mmol/L) among high-risk patients (n=1945; 80% of the overall population)

Variable	Adjusted OR (95% CI)	P
Age, per 1-year increase	0.98 (0.97–0.99)	<0.0001
Women	1.32 (1.08–1.61)	0.0068
Current smoker	1.22 (0.92–1.61)	0.1646
Sedentary lifestyle	1.02 (0.84–1.24)	0.8482
Body mass index ≥30 kg/m^2	1.02 (0.82–1.28)	0.8457
Waist circumference >102 cm (men), >88 cm (women)	0.97 (0.77–1.22)	0.7685
Hypertension	0.95 (0.75–1.19)	0.6401
Diabetes mellitus	0.46 (0.37–0.57)	<0.0001
Ischemic heart disease	0.66 (0.53–0.81)	<0.0001
Cerebrovascular disease	0.89 (0.65–1.20)	0.4371
Peripheral artery disease	1.10 (0.80–1.51)	0.5498

TABLE 5
Multivariable analysis: Factors associated with lack of achievement of both target low-density lipoprotein cholesterol (ie, greater than 2.0 mmol/L) and total cholesterol/high-density lipoprotein cholesterol ratio (ie, greater than 4) among high-risk patients (n=1945; 80% of the overall population)

Variable	Adjusted OR (95% CI)	P
Age, per 1-year increase	0.96 (0.95–0.98)	<0.0001
Women	0.80 (0.62–1.04)	0.0951
Current smoker	1.41 (1.03–1.93)	0.0337
Sedentary lifestyle	1.38 (1.08–1.76)	0.0110
Body mass index ≥30 kg/m^2 (obesity)	1.15 (0.86–1.52)	0.3436
Waist circumference >102 cm (men), >88 cm (women)	1.19 (0.89–1.60)	0.2399
Hypertension	0.97 (0.73–1.30)	0.8598
Diabetes mellitus	0.59 (0.45–0.77)	0.0001
Ischemic heart disease	0.62 (0.47–0.80)	0.0003
Cerebrovascular disease	1.05 (0.72–1.55)	0.7979
Peripheral artery disease	0.97 (0.65–1.45)	0.8969

studies demonstrating benefit of those agents using a higher versus a lower dose or versus other less potent statins. Furthermore, only 14% received an additional lipid-lowering agent in our observational study. Thus, based on the results of the main DYSIS study (data not shown) and the Canadian cohort, the vast majority of patients not at target were on low-to-medium doses of statins and, thus, there was an opportunity for upward titration as the initial step rather than addition of a second drug. It has previously been noted that only a minority of undertreated patients not achieving treatment targets experienced documented drug intolerance or side effects (4). Furthermore, a strategy employing an algorithm-based statin uptitration followed by the addition of ezetimibe was useful to further LDL-C lowering where statin monotherapy had not achieved target lipid values; attainment of an LDL-C target increased with consecutive visits (63%, 67% and 71% at the second, third and final visits, respectively) (5). While the value of ezetimibe in reducing adverse cardiovascular outcomes remains unproven, these findings highlight the potential opportunities to improve guideline-recommended target achievement in the Canadian context.

The observations that older age and male sex were independent predictors of treatment success are consistent with those observed in Canadian (4,5), American (10,11) and international (12) settings. Even after adjusting for age and other factors – in fact, older patients were more likely to achieve target LDL-C and both target LDL-C and TC/HDL-C ratio – women were less likely to be at the Canadian guideline-recommended LDL-C goal, suggesting that previously documented sex disparities in the management of dyslipidemia appear to persist (4,5,7,12). However, it remains unclear whether these differences are due to a sex bias because there are likely unmeasured confounders that have not been accounted for. Also, women in DYSIS were more frequently 'lower risk' (ie, without established vascular disease) compared with men, and their physicians may not have been as aggressive in attempting to achieve target cholesterol goals in this lower (but still at-) risk population.

A paucity of clinical outcome data from therapeutic approaches directly targeting HDL-C (and TC/HDL-C ratio) and triglycerides are highlighted by the observation that while low HDL-C, high TC/HDL-C ratio and/or elevated triglycerides were found in approximately three, two and four of every 10 patients in the present study, respectively, less than 5% of patients were receiving treatments that were specifically directed toward HDL-C and triglycerides. This suggests both a future need for and potential benefit of multitargeted treatment strategies that could address the full range of lipid abnormalities, while acknowledging that the evidence base to date primarily addresses LDL-C management.

Limitations

Our study has several limitations that should be addressed. First, DYSIS was a cross-sectional (single-point), observational study that did not evaluate long-term outcomes; therefore, any risk estimates were calculated based on current or retrospective data, rather than observed prospectively. Second, lipid parameters were those taken from patient medical records without routine blood sample collection or central, core-laboratory evaluation; however, DYSIS reflects a more 'real-world' practice in which physicians would initiate and titrate therapy based on test results available to them in their routine practice. In addition, we did not undertake local monitoring of source documents to confirm the accuracy of the data transcribed from the patient's medical record into the case report form. Third, given that current statin use was a patient eligibility criterion, we may have overestimated the impact of statin use on target levels across a broader high-risk population. Fourth, our study did not collect details regarding patient lifestyle, their genetic

predisposition to cardiovascular disease (although family history was assessed), history of side effects while on statins or treatment adherence. Fifth, while our study attempted to minimize bias by asking physicians to enrol consecutive eligible patients, the nonrandom selection and requirement for consent limits the generalizability of our findings. Furthermore, we cannot confirm that the physicians (who volunteered to participate in the registry) are representative of Canadian practice. We also cannot determine the impact of this selection bias given that nonparticipating physicians and their patients may be even less likely to follow treatment guidelines and attain targets. Sixth, we did not collect lipid profiles obtained before initiation of statin therapy and are, therefore, unable to assess the percentage reduction achieved following treatment initiation; the most recent (2009) Canadian guidelines recommend that an LDL-C target of less than 2.0 mmol/L or a 50% reduction in LDL-C are the desired goals. Furthermore, the study was undertaken before the most recent Canadian guidelines were published and we can only speculate on their direct relevance to current practice; however, the even lower current LDL-C target would suggest that the treatment gap may be even larger in contemporary practice. Seventh, because the most recent lipid profile obtained could be up to six months old with respect to the inclusion visit and the patient's statin dose had to be stable for more than three months, it is possible that some patients had their dose of statin increased following their last blood test but had still not yet undergone repeat lipid profile testing on the new statin dose.

SUMMARY

The present Canadian observational study highlights the need for more optimal treatment of lipid abnormalities, particularly among high-risk patients. More recent studies, supported by updated Canadian guideline recommendations (13), have demonstrated that even a more aggressive lowering of LDL may be warranted. Thus, the need to titrate current statin therapy to higher doses, potentially use a combination of lipid-modifying treatments (as seen in the optimal management of hypertension) once the statin dose has been truly maximized, and optimize adherence is paramount to further bridge the gap between evidence-based medicine and current Canadian practice.

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CONFLICTS OF INTEREST: The authors (except for S Goodman) received consultant fees in relation to their role as DYSIS Scientific Committee members. SG Goodman has received research grant support and speaker/consulting honoraria from Merck Frosst Canada Ltd, AstraZeneca Canada Inc and Pfizer Canada. A Langer has received research grant support and speaker/consulting honoraria from Merck Frosst Canada Ltd, AstraZeneca Canada Inc and Pfizer Canada. N Bastien is an employee of Merck Frosst Canada Ltd. R McPherson has received research grant support from Pfizer Canada and speaker/consulting honoraria from AstraZeneca Canada Inc, Merck Frosst/Schering Pharmaceuticals (Canada), Pfizer Canada and Solvay Pharmaceuticals Inc (USA). GA Francis has received research grant support from Pfizer Canada and speaker/consulting honoraria from AstraZeneca Canada Inc, Merck Frosst/Schering Pharmaceuticals (Canada), Pfizer Canada, Sepracor Inc (USA) and Solvay Pharmaceuticals Inc (USA). J Genest has received research grant support and speaker/consulting honoraria from AstraZeneca Canada Inc, GlaxoSmithKline Inc (Canada), Merck Frosst Canada Ltd, Pfizer Canada and Resverlogix Corp (Canada). LA Leiter has received research grant support and speaker/consulting honoraria from AstraZeneca Canada Inc, Merck Frosst Canada Ltd, Pfizer Canada, Roche Canada and Solvay Pharmaceuticals Inc (USA).

APPENDIX

Canadian DYSIS Investigators

Alberta: Grace M Bokenfohr, Edmonton; Edmond KH Liu, Calgary; Gordon W Melling, Calgary; Edward W Papp, Edmonton; Ashok K Sachdeva, Calgary; Ernst R Snyman, Camrose; Sonya Varma, Calgary; Richard A Ward, Calgary; Andrew PT Wong, Edmonton.

British Columbia: Paul J Basson, Chilliwack; Brian D Brodie, Chilliwack; Sukhjiwan J Chahal, Chilliwack; William Y Chan, Abbotsford; John C Chow, Chilliwack; Maura Cormack, North Vancouver; Donald HJ Eddy, Coquitlam; Daniel Ezekiel, Vancouver; Andrew Farquhar, Kelowna; Shian Gu, Burnaby; Ting H Hii, Trail; Marianne PK Ho-Asjoe, Vancouver; Andrew Hosie, Sidney; Shahin Jaffer, Delta; Andrew T Jakubowski, Richmond; Mandy Karim, Vancouver; Cristina Kiai, North Vancouver; Jacobus Kooy, Penticton; Craig R Lytle, Maple Ridge; Kevin L McLeod, North Vancouver; Stephen M Milne, Coquitlam; David C Morgan, Victoria; Michael M Myckatyn, Richmond; John PY Ng, Burnaby; Ronnald Schriemer, Kelowna; Gerhard Schumacher, Kamloops; James G Stopforth, Chilliwack; Winston WH Tsui, Maple Ridge; Robin T Wilson, Langley; Danny Wong, Richmond; Wilfred T Wong, Coquitlam; Margaret MW Yeung, Richmond.

Manitoba: David H Cram, Souris; Dilani TK Dissanayake, Winnipeg; Johan DW Gerber, Winnipeg; David Haligowski, Winnipeg; Blair Hrabarchuk, Dauphin; Tadeusz J Kroczak, Winnipeg; Alan H Lipson, Winnipeg; Raj K Mahay, Winnipeg; Abraham CW Mare, Winnipeg; Feisal J Mohamdee, Stonewall; Frederick T Olynyk, Winnipeg; Ramanbhai C Patel, Gimli; Wickus Pieterse, Russell; Rajendranath Ramgoolam, Winnipeg; Anna Rothova, Winnipeg; Kevin K Saunders, Winnipeg; Stanley Szajkowski, Winnipeg; Richard F Van Gend, Lac Du Bonnet; Nicolaas MJ Van Rensburg, Brandon.

New Brunswick: Sanjiv Anand, Dieppe; Carolyn EH Baer, Moncton; Eric JY Basque, Pointe Des Robichaud; Sebastian Benaya, Miramichi; Ricardo Bessoudo, Saint John; Jaswinder Bhalla, Moncton; Nataraj V Chettiar, Bathurst; Brian N Craig, Saint John; France Desrosiers, Pointe Des Robichaud; Manel R Imbulgoda, Fredericton; Gareth M Morgan, Nackawic; Zbigniew J Nowak, Miramichi; Daniel G Scott, Grand Bay-Westf; Gregory R Searles, Saint John; J Ninian Slorach, Miramichi; Robert N Stevenson, Sussex.

Newfoundland and Labrador: Noel J Browne, St John's; Karl J Bruff, Stephenville; John M Collingwood, St John's; Wayne Collins, Lewisporte; Aidan Drover, Carbonear; Anthony M Gabriel, Gander; Moonsamy Govender, Gander; David G Hart, St John's; Lydia B Hatcher, Mount Pearl; John Janes, Mount Pearl; John F Kielty, Deer Lake; Michoke Krisdaphongs, Conception Bay South; Richard B Lush, Grand Falls-Windsor; William B Moulton, Marystown; Cyril R Riche, Mount Pearl; Gary M Rideout, Mount Pearl; Bernard C Roberts, Marystown; Paul E Walsh, Holyrood; Harold G Wight, St John's; K Heather Woodland, St John's; Robert C Woodland, St John's.

Nova Scotia: Bradley C Atkinson, Sheet Harbour; Carlyle SHA Chow, Baddeck; James A Collins, Port Hawkesbury; Robert D Graham, Truro; Jalal Hosein, Halifax; Teresa M Machel, Windsor; Gordon R Mahaney Jr, Dartmouth; James RB McLean, Hubbards; Michael R Murray, Truro; Gregory A Myatt, Mira Road; Christopher P Ozere, Dartmouth; Amal K Saha, Bridgewater; David H Sanders, Dartmouth; Donald M Seaman, Kentville; James G Seaman, Kentville; Deanna Swinamer, Halifax; Kenny YV Yee, Barrington Passage.

Ontario: Mohamed M Ali, Welland; Clarence DC Bankay, Hamilton; Eitel ER Beduhn, Sault Ste Marie; Denis J Callaghan, Hamilton; Yun K Chan, Niagara Falls; Arif R Chaudhri, Toronto; Richard YY Chen, Mississauga; James R Conway, Smiths Falls; William L Cunningham, Belleville; Steven L Cusimano, Hamilton; Eleanor De Souza, Nepean; Selwyn X De Souza, Ottawa; Francis S Demarco, Windsor; J Paul DeYoung, Cornwall; Ralph Epstein, Hamilton; Alan A Faiers, Toronto; Victor J Figurado, Mississauga; FBT Forbes, Brampton; Zsuzsanna Gabor, Scarborough; Rodolfo C Gallardo, Etobicoke; Shiva K Gaur, Scarborough; Elizabeth George, Scarborough; Brian J Hartford, Thunder Bay; Michael SC Ho, Toronto; Shiraz H Ismail, Toronto;

Bharat B Kalra, Scarborough; Kinga Koprowicz, Kirkfield; Naresh Kumar, Cobourg; Clement Lam, Etobicoke; Ming-Jarm Lau, North York; Hugo KC Law, Scarborough; Max Leung Sui Fung, Oshawa; Joanne F Liutkus, Cambridge; Talaat K Lotfallah, Kingston; Robert G Luton, London; Gloria S Meneses, Scarborough; Mark L Miller, Jarvis; Noorbegum Nagji, Toronto; Ken HM Ng, Markham; Roland E Ng Thow Hing, Pembroke; Amritanshu S Pandey, Cambridge; Ivan Petrov, Toronto; Wendy Rosenthall, Mississauga; Howard Rudner, Toronto; Alan D Russell, Leamington; Zenia A Sanchez, Mississauga; Joseph A Shaban, Windsor; Shiraz BK Shariff, Brampton; Chung Ming Shih, Woodbridge; Duncan W Sinclair, Aylmer; Donald R Spink, Peterborough; Tommy Hak Tsun Tung, Keswick; Saul Vizel, Cambridge; David F Yanover, Hamilton; Louis S Zavodni, Hamilton.
Prince Edward Island: Paul Cusack, Charlottetown; Charles M Dewar, O'Leary; Peter Hooley, Charlottetown; Rachel A Kassner, Charlottetown; Randy J MacKinnon, Charlottetown; Harold W Molyneaux, Summerside; Karunakara N Shetty, Charlottetown.
Québec: Ginette Barrière, Sainte-Catherine; Maria B Berjat, Ville St-Laurent; Bruno Bernucci, Saint-Léonard; Claude Bérubé, Chicoutimi; Ghyslain Boudreau, Québec; Raja Chehayeb, Greenfield Park; Domenico Ciricillo, Saint-Léonard; Christian M Constance, Montréal; Gilles Côté, Montréal; Jacques Desroches, Saint-Pie; Robert Gagnon, Clermont; Gilles Gaudreau, Sorel-Tracy; Jean Louis Godbout, Gatineau; Pierre Harvey, Chicoutimi; Youssef Hassan, Trois-Rivières; Ngoc Vinh Hoang, Anjou; Danielle Houde, Courcelette; Alain-Paul Lalonde, Saint-Bruno-Lac-Saint-Jean; Régis Lavoie, Alma; Normand Leclair, Trois-Rivières; Luc Meagher, Saint-Charles-Borromée; Alain Ouimet, Sainte-Adèle; Simon Plourde, Rouyn Noranda; Denis W Rioux, Québec; Claude Roberge, Saint-Stanislas-De-Champlain; Bruno Roy, Beauceville; Richard Sasseville, Dolbeau-Mistassini; Samuel Serfaty, Montreal; Lyne Theriault, Princeville; Jean R Timothée, Greenfield Park; Sabine Tjia, Lasalle; Bruno Tremblay, Québec; Jean Turcotte, Valcourt.
Saskatchewan: Sabyasachi Bose, Saskatoon; Hester A Bouwer, Regina; Patricia A Chernesky, Nipawin; Mervin L Johnson, Meadow Lake; David R Kemp, Wilkie; Raymond PC Lai, Regina; Frank R Lee, Yorkton; William GC Lipsett, North Battleford; Schalk J Lombard, Prince Albert; Falah S Majid, Moose Jaw; Johannes J Malan, Watrous; Narinda Maree, Craik; Arun Nayar, Saskatoon; Mandi Nel, Esterhazy; Oluwole O Oduntan, Yorkton; Alphonsus RJ Rajakumar, Saskatoon; Fauzi B Ramadan, Moose Jaw; Mohammed Shamsuzzaman, Regina; Abraham PM Vermeulen, Regina; C Fred Wigmore, Moose Jaw.

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