



Original Article

GOAL Canada: Physician Education and Support Can Improve Patient Management

Anatoly Langer, MD, MSc, FRCP,^a Mary Tan, MSc, CCRP,^a

Shaun G. Goodman, MD, MSc, FRCP,^{a,b} Jean Grégoire, MD, FRCP,^c Peter J. Lin, MD, CCFP,^a

G. B. John Mancini, MD, FRCP,^d James A. Stone, MD, PhD, FRCP,^e Cheryl Wills, CCRP,^a

Caroline Spindler, CCRP,^a and Lawrence A. Leiter, MD, FRCP^f

^a Canadian Heart Research Centre, North York, Ontario, Canada

^b St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada

^c Interventional Cardiologist, Institut de Cardiologie de Montréal, Université de Montréal, Montreal, Quebec, Canada

^d St Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada

^e Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

^f Li Ka Shing Knowledge Institute, St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada

ABSTRACT

Background: Despite the widespread use of statins, approximately 40% to 50% of Canadian patients with known cardiovascular disease do not achieve the low-density lipoprotein cholesterol (LDL-C) goal. **Guidelines Oriented Approach to Lipid lowering (GOAL)** is an investigator-initiated study aiming to ascertain the use of second- and third-line therapy and its impact on LDL-C goal achievement in a real-world setting.

Methods: GOAL enrolled patients with clinical vascular disease or familial hypercholesterolemia and LDL-C > 2.0 mmol/L despite maximally tolerated statin therapy. During follow-up, physicians managed patients as clinically indicated but with online reminders of guideline recommendations.

RÉSUMÉ

Contexte : Malgré l'utilisation répandue des statines, environ 40 à 50 % des patients canadiens atteints d'une maladie cardiovasculaire connue n'atteignent pas les taux cibles de cholestérol à lipoprotéines de basse densité (C-LDL). L'étude GOAL (*Guidelines Oriented Approach to Lipid lowering*) est une étude entreprise par un chercheur afin d'évaluer, en contexte réel, l'utilisation de traitements de deuxième et de troisième intention et les effets de ceux-ci sur l'atteinte des taux cibles de C-LDL.

Méthodologie : Des patients atteints d'une maladie vasculaire clinique ou d'une hypercholestérolémie familiale, présentant un taux de C-LDL > 2,0 mmol/l malgré un traitement par une statine à la dose maximale tolérée, ont été inscrits à l'étude GOAL. Pendant la période

Low-density lipoprotein cholesterol (LDL-C) is a well-established risk factor for cardiovascular (CV) disease, and there is considerable evidence that lowering LDL-C reduces the risk of both CV events and mortality in patients with CV disease.¹ Nonetheless, strategies for lowering LDL-C are often poorly adopted in clinical practice, and many patients fail to reach guideline-recommended levels.^{2–10} Thus, patients in routine practice may not receive similar benefits in CV risk

reduction to those observed in clinical trials. Although statins remain the mainstay of dyslipidemia management, attainment of the recommended LDL-C levels can be difficult without use of combination therapy.¹¹

In the Canadian Heart Research Centre Diabetes Mellitus Status in Canada (DM-SCAN) survey,¹² only 57% of patients with high CV risk and diabetes achieved the guideline-recommended LDL-C level of < 2.0 mmol/L. Likewise, in the Canadian cohort of the **Dyslipidemia International Study (DYSIS Canada)**, only 63% of all patients with high CV risk had the recommended LDL-C levels.¹³ Even in a recently completed Alberta survey, 48.5% of patients with atherosclerotic CV disease receiving lipid-lowering treatment, with the majority on moderate/high-dose statin therapy, did not achieve an LDL-C < 2.0 mmol/L.¹⁴

The clinical implications of this type of care gap are significant and have been reported,¹⁵ providing projections for

Received for publication November 8, 2019. Accepted December 4, 2019.

Ethics Statement: Research reported here adhered to the relevant ethical guidelines.

Corresponding author: Dr Anatoly Langer, University of Toronto, Canadian Heart Research Centre, 259 Yorkland Road, Toronto, Ontario M2J 0B5, Canada. Tel.: +1-416-977-8010 ext 253; fax: +1-866-562-9769.

E-mail: LangerA@chrc.net

See page 53 for disclosure information.

Results: Of 2009 patients enrolled (median age 63 years, 42% were female), baseline total cholesterol was 5.5 ± 1.4 mmol/L, LDL-C was 3.3 ± 1.3 mmol/L, non-high-density lipoprotein cholesterol was 4.1 ± 1.4 mmol/L, high-density lipoprotein cholesterol was 1.3 ± 0.4 mmol/L, and triglycerides were 2.0 ± 1.5 mmol/L. Lipid-lowering therapy used at baseline was statin therapy in 76% (with 24% statin intolerant) and ezetimibe in 25%. During follow-up, the proportion of patients achieving an LDL-C level of < 2.0 mmol/L increased significantly to 50.8% as a result of additional lipid-lowering therapy. Patients achieving the recommended LDL-C level were more likely to not be statin intolerant (83.8% vs 70.7%, $P < 0.0001$) and to be taking a high-efficacy type and dose of statin (52.4% vs 35.9%, $P < 0.0001$). The 3 top reasons for not using the recommended therapy with ezetimibe were patient refusal in 33%, not needed in 22%, and intolerance in 20%, whereas for PCSK9i the reasons were cost in 26%, not needed in 27%, or patient refusal in 25%.

Conclusion: The results indicate the feasibility of optimizing management, resulting in achievement of the guideline-recommended LDL-C level. This has the potential to translate into reductions in cardiovascular morbidity and mortality of Canadian patients.

the number of CV morbidity and mortality events that can be prevented if Clinical Practice Guidelines (CPGs) are followed.¹⁶ The CV benefits of add-on therapy for LDL-C lowering have recently been confirmed^{17–19} and incorporated into the Canadian practice.

Thus, this **Quality Enhancement Research Initiative (QuERI)** is an implementation science program²⁰ addressing the underlying reasons and solutions for clinical inertia with educational intervention based on feedback to physicians on their management of dyslipidemia to support their decision

de suivi, les médecins prenaient en charge le traitement de leurs patients selon les besoins cliniques, mais en recevant par voie électronique des rappels des recommandations formulées dans les lignes directrices.

Résultats : Chez les 2009 patients inscrits à l'étude (âge médian : 63 ans; femmes : 42 %), les taux initiaux moyens étaient les suivants : cholestérol total initial : $5,5 \pm 1,4$ mmol/l, C-LDL : $3,3 \pm 1,3$ mmol/l, C non HDL (autre que le cholestérol à lipoprotéines de haute densité) : $4,1 \pm 1,4$ mmol/l, C-HDL (des lipoprotéines de haute densité) : $1,3 \pm 0,4$ mmol/l et triglycérides : $2,0 \pm 1,5$ mmol/l. Le traitement hypolipémiant utilisé au début de l'étude était composé d'une statine chez 76 % des participants (24 % des patients ne toléraient pas les statines) et d'ézétimibe chez 25 %. Pendant la période de suivi, la proportion de patients atteignant un taux de C-LDL $< 2,0$ mmol/l a augmenté de façon significative, jusqu'à atteindre 50,8 %, en raison de l'utilisation d'hypolipémiants additionnels. Les patients atteignant les taux cibles de C-LDL étaient plus susceptibles de ne pas être intolérants aux statines (83,8 % vs 70,7 %, $p < 0,0001$) et de prendre un type et une dose de statine hautement efficaces (52,4 % vs 35,9 %, $p < 0,0001$). Les trois principales raisons évoquées pour expliquer le fait de n'avoir pas eu recours au traitement recommandé par l'ézétimibe étaient le refus du patient (33 %), l'absence de besoin (22 %) et l'intolérance (20 %), alors que dans le cas des inhibiteurs de la PCSK9, les raisons données étaient plutôt le coût élevé (26 %), l'absence de besoin (27 %) et le refus du patient (25 %).

Conclusion : Les résultats de cette étude montrent la faisabilité de l'optimisation de la prise en charge, qui entraîne l'atteinte des taux de C-LDL recommandés dans les lignes directrices. Ces résultats pourraient se traduire par des réductions de la morbidité et de la mortalité d'origine cardiovasculaire chez les patients canadiens.

making and choice of therapy to more optimally achieve the guideline-recommended LDL-C level in high-risk patients.²¹

Methods

The **Guidelines Oriented Approach to Lipid Lowering (GOAL) Canada** was an interventional program supported by Amgen Canada as an investigator-initiated study started in 2015 and coordinated by the Canadian Heart Research Centre, an academic research and education physician

Table 1. Comorbid conditions at baseline and in those achieving or not achieving the recommended LDL-C level

	Overall (N = 2009)	LDL-C target not achieved at last available visit (N = 1138)	LDL-C target achieved at last available visit (N = 871)	P
Age (y) [†]	63 (55, 71)	62 (55, 71)	63 (56, 70)	0.12
Gender, male	57.9%	51.6%	66.3%	< 0.0001
BMI (kg/m ²) [†]	28.7 (25.4, 32.3)	28.4 (25.1, 32.1)	28.9 (26.0, 32.5)	0.012
Systolic blood pressure (mm Hg) [†]	128 (120, 138)	128 (120, 140)	128 (120, 136)	0.27
Diastolic blood pressure (mm Hg) [†]	78 (70, 82)	78 (70, 82)	78 (70, 81)	0.32
Coronary artery disease	51.6%	44.2%	61.2%	< 0.0001
Cerebrovascular disease	8.2%	8.3%	8.2%	0.93
Peripheral arterial disease/abdominal aortic aneurysm	10.3%	9.8%	11.0%	0.35
FH*	47.5%	49.8%	44.6%	0.019
Hypertension	60.2%	57.1%	64.3%	0.001
Smoking history	48.1%	44.7%	52.5%	0.0006
Diabetes mellitus	35.2%	34.4%	36.3%	0.39
Chronic kidney disease	8.1%	9.3%	6.5%	0.024

* In those with FH, 16% also had CV disease.

[†] Median (25th, 75th) percentiles.

Table 2. Cardiovascular medications and in those achieving or not achieving the recommended LDL-C level

	Overall (N = 2009)	LDL-C target not achieved at last available visit (N = 1138)	LDL-C target achieved at last available visit (N = 871)	P
ACE inhibitor	38.2%	34.1%	43.5%	< 0.0001
Angiotensin receptor blockers	22.4%	22.9%	21.8%	0.58
Beta-blocker	39.1%	33.6%	46.4%	< 0.0001
Calcium channel blocker	22.4%	21.1%	24.0%	0.12
Diuretic	19.0%	20.3%	17.2%	0.08
Antiplatelet therapy	61.3%	55.5%	68.8%	< 0.0001
Anticoagulant therapy	7.2%	7.2%	7.2%	0.98

ACE, angiotensin-converting enzyme; LDL-C, low-density lipoprotein cholesterol.

organization. The intervention studied was physician education on the implementation of Canadian guidelines.¹⁶ The educational intervention was applied at the end of each visit on the basis of data entry in the electronic case report form. Specifically, physicians were asked if they would add LDL-C-lowering therapy as recommended by the CPGs.¹⁶ If the management chosen was consistent with the recommendations,¹⁶ then no further intervention was applied. If the management chosen was not consistent with the recommendation, physicians were alerted to that as an extra screen shown in the electronic case report form and asked if they would modify their management, and if not to provide the most significant single reason as to why not. The primary end point was the proportion of patients achieving the CPG¹⁶ recommended level for LDL-C at the last available follow-up visit. The study was approved by central and institutional Research Ethics Board where appropriate, and all enrolled patients provided informed consent.

Invitations to participate were sent to 750 Canadian physicians across Canada from a proprietary Canadian Heart Research Centre list of physicians who participated in prior cholesterol-oriented data-collection exercises,^{12,13,21} and 248 were activated to enroll their patients. These physicians were asked to enroll at least 12 of their patients with clinical vascular disease, such as coronary artery disease, cerebrovascular disease, abdominal aortic aneurysm, or peripheral arterial disease, or familial hypercholesterolemia (FH) as defined in the CPG.¹⁶ Patients also had to have LDL-C > 2.0 mmol/L despite maximally tolerated statin therapy (defined as having tried at least 2 statins, each at least on 2 reduced doses) for the last 3 months before enrollment. Physicians were asked to

enroll sequential patients, although it is not possible to verify this. Exclusion criteria were participation in a clinical trial with masked (blinded) cholesterol-lowering therapy, ongoing treatment with PCSK9i, or prior participation in the GOAL Canada program. Levels of LDL-C and management thereof were assessed on 3 occasions: baseline and twice more approximately 4 to 6 months apart.

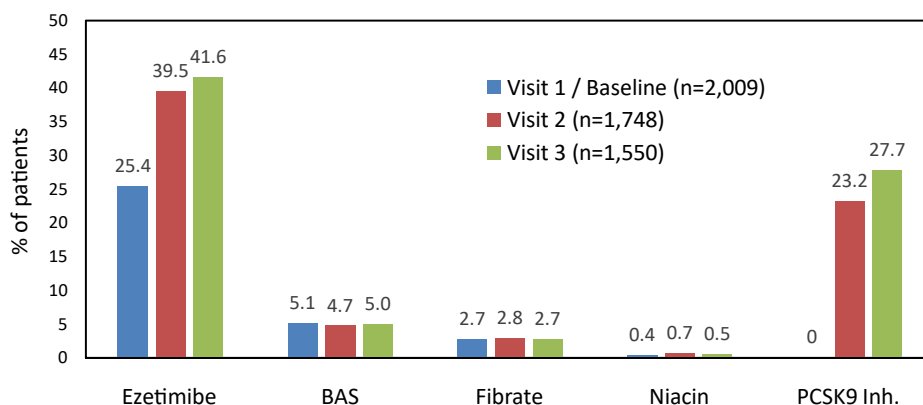
The sample size of 2500 patients was planned for on the basis of the experience and success with the DYSIS registry in Canada.¹³ The study was stopped prematurely when the investigator-initiated study grant was exhausted mainly because of the longer duration of enrollment. The prespecified primary end point was the proportion of patients achieving the recommended LDL-C level of < 2.0 mmol/L.

Statistical analysis

Continuous data are shown as means with standard deviation or medians with 25th and 75th percentiles, and categorical data are shown as frequencies and percentages. Group comparisons were made using the chi-square test or McNemar test and paired *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.

Results

The GOAL Canada study stopped recruitment on December 31, 2018, and last follow-up on September 30, 2019. In total, 248 physicians across Canada (60% primary



BAS = bile acid sequestrant

Figure 1. The use of lipid-lowering therapy beyond statin therapy at baseline and during follow-up. BAS, bile acid sequestrant.

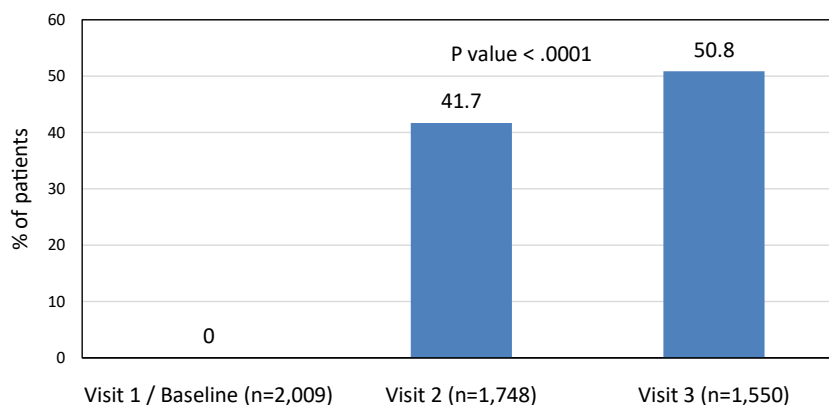


Figure 2. Proportion of patients achieving the recommended low-density lipoprotein cholesterol (LDL-C) level during follow-up (primary end point).

care and 40% specialists) were registered to participate, and 2027 patients were enrolled (58% were men; median age, 63 years): British Columbia, 169 patients; Alberta, 90 patients; Saskatchewan, 6 patients; Manitoba, 49 patients; Ontario, 1545 patients; Quebec, 108 patients; New Brunswick, 41 patients; and Nova Scotia, 19 patients. There were 18 patients whose enrollment violated protocol inclusion criteria, and these were removed from analysis. During follow-up for visit 2 (141 ± 133 days after enrollment) and visit 3 (176 ± 145 days after visit 2), 5 and 4 patients died, 45 and 21 patients withdrew consent, and 214 and 184 patients were lost to follow-up, respectively. In total, 2009 patients were followed, and their results are reported.

Demographic variables and comorbid conditions are summarized in Table 1, and CV medications are shown in Table 2, including the comparison based on whether the recommended LDL-C level was achieved. Those patients achieving the LDL-C < 2 mmol/L were more likely to have coronary artery disease (along with CV medications) rather than FH, to be male and hypertensive, and to have a history of smoking or chronic kidney disease.

Baseline total cholesterol was 5.5 ± 1.4 mmol/L, LDL-C was 3.3 ± 1.3 mmol/L, non-high-density lipoprotein cholesterol was 4.1 ± 1.4 mmol/L, high-density lipoprotein cholesterol was 1.3 ± 0.4 mmol/L, and triglycerides were 2.0 ± 1.4 mmol/L. LDL-C was 3.0 ± 0.9 mmol/L among those with CV disease alone, 3.9 ± 1.5 mmol/L in those with FH alone, and 3.4 ± 1.3 mmol/L in those with both.

Lipid-lowering therapy used at baseline was statin therapy in 76% (with 24% statin intolerant) and ezetimibe in 25%. Statins used most frequently were rosuvastatin (40%, mean daily dose 22 mg) and atorvastatin (28%, mean daily dose 48 mg). Patients achieving the recommended LDL-C level were more likely to not be statin intolerant (83.8% vs 70.7%, $P < 0.0001$) and to be on high efficacy type and dose of statin (52.4% vs 35.9%, $P < 0.0001$).

The use of additional lipid-modifying therapies during follow-up and the increase in the addition of recommended therapies (specifically the use of ezetimibe and PCSK9i) are shown in Figure 1. The proportion of patients achieving the Canadian Cardiovascular Society recommended LDL-C level of < 2.0 mmol/L (primary end point) increased significantly to 41.7% and 50.8% in visits 2 and 3, respectively (Fig. 2). The mean LDL was 3.3 mmol/L at baseline (visit 1) and decreased significantly to 2.4 and 2.2 mmol/L, respectively, during the follow-up in visits 2 and 3 (Fig. 3).

Achievement of the recommended LDL-C level was associated with a more frequent use of recommended lipid-lowering therapy at the last available visit with ezetimibe (44.4% vs 33.0%, $P < 0.0001$) and PCSK9i (38.6% vs 11.0%, $P < 0.0001$). The reasons for not using the recommended therapy after the initial visit are shown in Table 3. The proportion of patients in whom physicians indicated at baseline that addition of ezetimibe was not needed achieved recommended LDL-C level less frequently than those for whom the decision was made to prescribe it during the next

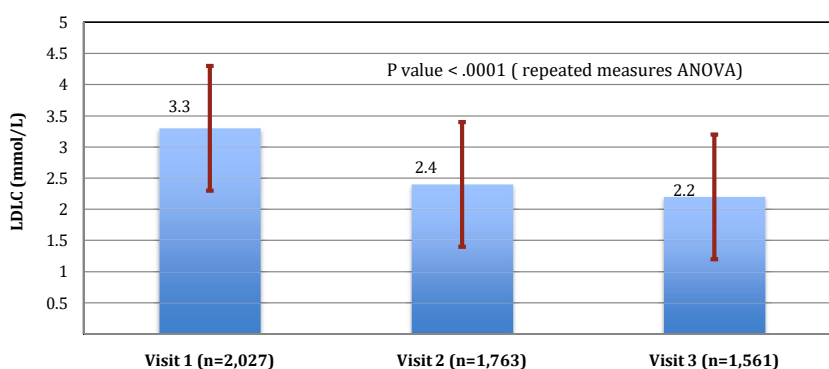


Figure 3. LDL-C at baseline and during follow-up. ANOVA, analysis of variance; LDL-C, low-density lipoprotein cholesterol.

Table 3. Reasons provided by physicians for not changing therapy according to the guideline-based recommendations

Reasons “why not”	PCSK9 inhibitor			Ezetimibe		
	Visit 1/baseline (N = 947)	Visit 2 (N = 811)	Visit 3 (N = 671)	Visit 1/baseline (N = 915)	Visit 2 (N = 583)	Visit 3 (N = 461)
Not needed	27.1	20.7	18.9	22.1	20.4	22.1
Patient refused	24.8	41.2	44.1	32.5	40.5	39.9
Will prescribe next visit	18.4	10.9	6.9	14.0	8.4	5.7
Cost	26.2	23.9	24.9	9.3	5.8	3.9
Comorbidities	1.1	0.7	2.2	1.2	1.4	1.5
Patient intolerant	1.5	2.2	3.0	20.5	23.2	26.5
Social constraint	0.6	0.4	0	0.1	0	0.2
Believe management is appropriate	0.3	0	0	0.3	0.3	0.2

Number is expressed as percentage based on available (N) reasons.

visit (34.7% vs 53.9%, $P = 0.0006$). The same comparison with respect to the use of PCSK9i did not show a difference (45.5% vs 46%, $P = 0.93$).

Discussion

In patients with established CV disease, LDL-C lowering is one of the safest and efficient ways of lowering the risk of future CV events, including CV and total mortality and myocardial infarction and stroke. Lowering of LDL-C by 1 mmol/L results in 20% reduction in CV mortality and 12% reduction in total mortality, as well as 22% reduction in all CV events over 5 years.¹ Thus, a mean reduction of LDL-C of > 1 mmol/L observed in GOAL Canada (Fig. 3), if sustained, has the potential to provide an important reduction of CV death. More than half of high-risk patients could experience the risk of CV event reduced significantly by achieving the recommended LDL-C level as a result of physician reminder.

On enrollment, 24% of patients were not on any statin therapy because of intolerance. The etiology of treatment inertia can be multifactorial, including a number of patient- and physician-associated factors.²² We and others^{15,23–25} have demonstrated that treatment inertia is associated with unfavourable outcomes. The results of GOAL Canada indicate that both gaps in knowledge (eg, risk underestimation) and action (eg, “knowing the right thing but not doing it”) are present (Tables 1–3). Physician responses such as “additional treatment not needed” indicate a knowledge gap in approximately 20% of physicians and were associated with a significantly smaller proportion of patients achieving the recommended LDL-C level. On the other hand, the response “I will add therapy next visit” is indicative of an action gap in approximately 15% to 20% of physicians.

The impact of programs such as GOAL Canada is significant given the LDL-C reduction demonstrated and expected reduction in CV events associated with this lowering. Thus, clinician-oriented support tools addressing both knowledge and care gaps may be of value as an extension of professional guidelines, although widespread implementation of such approaches and cost-effectiveness have not been demonstrated. Application of the results from clinical trials as part of a general implementation science strategy suggests important and reasonably inexpensive benefits that may be realized by programs such as GOAL Canada. Some of this benefit is clearly generalizable to other physician practices in

Canada and may be realized by leveraging already implemented (and paid for) use of electronic medical records as a platform for clinical decision-making support.

Study limitations

Selection bias at the physician and patient level may limit the generalizability of our findings. The educational intervention was not applied at the time of the clinical encounter itself, that is, it was possible for physicians to enter the data at some later point. This was the reason for one of the choices being, “I will follow the guidelines during the next visit.” However, this does not detract from our overall implementation goal as demonstrated by clinically relevant increases in the proportion of patients achieving the guideline-recommended LDL-C level. Physician exposure to the educational intervention was not randomized; moreover, physicians may have received additional information or education regarding lipid lowering from other sources, which therefore limits the reliability or reproducibility of findings, and the results should be considered as hypothesis generating. A relatively short duration of follow-up did not allow assessment of the durability of the observed lowering in LDL-C levels.

Conclusion

The results of the GOAL Canada program indicate the feasibility of overcoming treatment inertia and improving LDL-C control, which should help to achieve reduction in CV morbidity and mortality of Canadian patients.

Funding Sources

There are no funding sources to disclose.

Disclosures

On behalf of the Canadian Heart Research Centre, A.L. has received research grant support from Actelion, Amgen, Bayer, BMS, Merck, Novo Nordisk, Pfizer, Servier, and Sanofi. L.A.L. has received research grant support from AstraZeneca, Amgen, Kowa, The Medicines Company, and Sanofi, and has served as a consultant for AstraZeneca, Amgen, Esperion, HLS, Merck, The Medicines Company, and Sanofi. J.G. has received speaker/consulting honoraria from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Ferring Pharmaceuticals, HLS Therapeutics, Janssen/Johnson

& Johnson, Merck, Novartis, Novo Nordisk, Pfizer, Sanofi, Servier, and Sunovion. S.G.G. has received research grant support (eg, steering committee or data monitoring committee) and/or speaker/consulting honoraria (eg, advisory boards) from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, CSL Behring, Daiichi-Sankyo, Eli Lilly, Esperion, Fenix Group International, Ferring Pharmaceuticals, GlaxoSmithKline, HLS Therapeutics, Janssen/Johnson & Johnson, Luitpold Pharmaceuticals, Matrizyme, Merck, Novartis, Novo Nordisk A/C, Pfizer, Regeneron, Sanofi, Servier, and Tenax Therapeutics; and salary support from the Heart and Stroke Foundation of Ontario/University of Toronto (Polo) Chair, Canadian Heart Research Centre and MD Primer, Canadian VIGOUR Centre, Duke Clinical Research Institute, New York University Clinical Coordinating Centre, and PERFUSE. J.A.S. has received research support from Sanofi and has served as a consultant and/or speaker for AstraZeneca, Amgen, Bayer, HLS Therapeutics Lilly, and Novartis. The remaining authors have no disclosures.

References

- Baigent C, Keech A, Kearney PM, et al; Cholesterol Treatment Trialists (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005;366:1267-78.
- Pearson TA, Laurora I, Chu H, Kafonek S. The Lipid Treatment Assessment Project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low density lipoprotein cholesterol goals. *Arch Intern Med* 2000;160:459-67.
- Waters DD, Brotons C, Chiang CW, et al. Lipid Treatment Assessment Project 2: a multinational survey to evaluate the proportion of patients achieving low-density lipoprotein cholesterol goals. *Circulation* 2009;120:28-34.
- Saposnik G, Goodman SG, Leiter LA, et al. Applying the evidence: do patients with stroke, coronary artery disease, or both achieve similar treatment goals? *Stroke* 2009;40:1417-24.
- Hackam DG, Leiter LA, Yan AT, et al. Missed opportunities for secondary prevention of cardiovascular disease in Canada. *Can J Cardiol* 2007;23:1124-30.
- Yan AT, Yan RT, Tan M, et al. Contemporary management of dyslipidemia in high-risk patients: targets still not met. *Am J Med* 2006;119:676-83.
- Banegas JR, Vegazo O, Serrano P, et al. The gap between dyslipidemia control perceived by physicians and objective control patterns in Spain. *Atherosclerosis* 2006;188:420-4.
- Ko DT, Mamdani M, Alter DA. Lipid-lowering therapy with statins in high risk elderly patients: the treatment-risk paradox. *JAMA* 2004;291:1864-970.
- Petrella RJ, Merikle E, Jones J. Prevalence and treatment of dyslipidemia in Canadian primary care: a retrospective cohort analysis. *Clin Ther* 2007;29:742-50.
- Rapezzi C, Biagini E, Bellis P, et al. Exploring the gap between National Cholesterol Education Program guidelines and clinical practice in secondary care: results of a cross-sectional study involving over 10 000 patients followed in different specialty settings across Italy. *J Cardiovasc Med* 2008;9:878-87.
- Martineau P, Gaw A, de Teresa E, et al. Effect of individualizing starting doses of a statin according to baseline LDL-cholesterol levels on achieving cholesterol targets: the Achieve Cholesterol Targets Fast with Atorvastatin Stratified Titration (ACTFAST) study. *Atherosclerosis* 2007;191:135-46.
- Leiter LA, Berard L, Bowering K, et al. Type 2 diabetes mellitus management in Canada: is it improving? *Can J Diabetes* 2013;37:277.
- Goodman SG, Langer A, Bastien NR, et al. Prevalence of dyslipidemia in statin treated patients in Canada: results of the Dyslipidemia International Study (DYSIS). *Can J Cardiol* 2010;26:e330-5.
- Chen G, Farris MS, Cowling T, et al. Treatment and low-density lipoprotein cholesterol management in patients diagnosed with clinical atherosclerotic cardiovascular disease in Alberta. *Can J Cardiol* 2019;35:884-91.
- Grima DT, Leiter LA, Goodman SG, et al. How many cardiovascular events can be prevented with optimal management of high-risk Canadians? *Can J Cardiol* 2008;24:363-8.
- Anderson TJ, Gregoire 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.
- Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med* 2015;372:2387-97.
- Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017;376:1713-22.
- Schwartz GG, Szarek M, Bhatt DL, et al. The ODYSSEY OUTCOMES Trial: Topline Results. Alirocumab in Patients After Acute Coronary Syndrome. Presented at the American College of Cardiology Annual Scientific Sessions, March 10, 2018; Orlando, Florida.
- Langer A, Tan M, Cieza T, et al. Can clinical reminder help optimize the use of secondary prevention therapies in non-ST elevation acute coronary syndrome? *Int J Cardiol Cardiovasc Med* 2017;1:1-5.
- Katz PM, Mendelsohn AA, Goodman SG, et al. Use of a treatment optimization algorithm involving statin-ezetimibe combination aids in achievement of guideline-based low-density lipoprotein targets in patients with dyslipidemia at high vascular risk Guideline-Based Undertaking to Improve Dyslipidemia Management in Canada (GUIDANC). *Can J Cardiol* 2011:138-45.
- Tsang JLY, Mendelsohn A, Tan MKK, et al. Discordance between physicians' estimation of patient cardiovascular risk and use of evidence-based medical therapy. *Am J Cardiol* 2008;102:1142-5.
- Rogers AM, Ramanath VS, Grzybowski M, et al. The association between guideline-based treatment instructions at the point of discharge and lower 1-year mortality in Medicare patients after acute myocardial infarction: the American College of Cardiology's Guidelines Applied in Practice (GAP) initiative in Michigan. *Am Heart J* 2007;154:461-9.
- Arnold SV, Spertus JA, Masoudi FA, et al. Beyond medication prescription as performance measures. *J Am Coll Cardiol* 2013;62:1791-801.
- Kucher N, Koo S, Quiroz R, et al. Electronic alerts to prevent venous thromboembolism among hospitalized patients. *N Engl J Med* 2005;352:969-77.