# Identifying and Bridging Treatment Gaps in the Management of Dyslipidemia

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One of the most important roles of primary-care physicians is the identification and optimal management of modifiable risk factors for cardiovascular disease (CVD). These risk factors are well known, and include smoking, dyslipidemia, hypertension, diabetes, obesity, sedentary lifestyle and poor nutrition.[1] Each of these individual risk factors needs to be addressed to provide optimal protection against the development or progression of CVD. To aid in this endeavor, multidisciplinary expert groups in Canada and around the world have developed evidence-based clinical practice guidelines that address each of these major risk factors.[1-4] These guidelines clearly identify which patients require treatment and specify the goals of therapy.

While healthcare professionals have done an excellent job over the past several decades in lowering CV-related mortality (rates of mortality from coronary artery disease, for example, have fallen 40% according to data from Statistics Canada[1]), much work remains to be done. Large population-based studies, as well as smaller, clinical-practice-based analyses, have shown that a substantial proportion of Canadian patients at risk for CVD do not have their risk factors treated to guideline-specified targets. This article reviews one such treatment gap, focusing on dyslipidemia.

## Treatment Targets for Dyslipidemia

The Canadian Cardiovascular Society (CCS) has recently updated its guidelines for the diagnosis and treatment of dyslipidemia.[1] The treatment targets from this 2009 update are summarized in Table 1. The authors specify that all patients deemed to be at high risk for CVD should be treated with lipid-lowering therapy to achieve a target low-density-lipoprotein cholesterol (LDL-C) of < 2.0 mmol/L or a reduction in LDL-C of 50% from baseline. Patients with moderate risk should also be treated to this same target, in the presence of: LDL-C > 3.5 mmol/L; total-cholesterol:HDL-C ratio > 5.0; or a high-sensitivity C-reactive protein (hsCRP) level of > 2 mg/L among men older than 50 years or women older than 60 years. Low-risk patients should be treated if their LDL-C is > 5.0 mmol/L, with a goal of reducing this parameter by 50%.

These recommendations continue the trend towards more aggressive treatment targets for dyslipidemia. In 2003, the recommended target LDL-C levels were < 2.5 mmol/L for high-risk patients, < 3.5 mmol/L for moderate-risk patients, and < 4.5 mmol/L for low-risk patients.[6] In the 2006 recommendations, for moderate- and low-risk patients, the goal was to lower LDL-C by at least 40%.[5]

These lower targets have arisen from clinical-trial data that have shown benefit of treatment to lower levels of LDL-C. At the same time, these trials have

TABLE 1. **Targets for the Treatment of Dyslipidemia: 2009 CCS Guidelines**[1]

| Risk level | Initiate treatment if: | Targets | |
|---|---|---|---|
| | | Primary: LDL-C | Primary alternate |
| **High**<br>• CAD, PVD, atherosclerosis<br>• Most patients with diabetes<br>• FRS > 20%<br>• RRS > 20% | Consider treatment in all patients | < 2 mmol/L<br>or 50% ↓<br>**(Class I, Level A)** | apo B < 0.80 g/L<br>**(Class I, Level A)** |
| **Moderate**<br>• FRS 10% to 19% | • LDL-C > 3.5 mmol/L<br>• TC:HDL-C ratio > 5.0<br>• hsCRP > 2 mg/L<br>– men > 50 years<br>– women > 60 years<br>*Note: Family history and hsCRP modulates risk (RRS)* | < 2 mmol/L<br>or 50% ↓<br>**(Class IIA, Level A)** | apo B < 0.80 g/L<br>**(Class I, Level A)** |
| **Low**<br>• FRS < 10% | LDL-C > 5.0 mmol/L | 50% ↓<br>**(Class IIA, Level A)** | |

CAD = coronary artery disease; PVD = peripheral vascular disease; FRS = Framingham Risk Score; RRS = Reynolds Risk Score.

also shown very good safety with this more aggressive strategy. Hence, the targets have been moved lower with each successive guideline reflecting the results of clinical trials such as PROVE-IT,[7] TNT[8] and JUPITER.[9]

## Treatment Gaps in Canada

How well are we doing in real-life practice in reaching these new targets? While the evidence has prompted the authors of clinical practice guidelines to become more stringent in their recommendations for treatment targets, there is also evidence that a large proportion of Canadian patients are not achieving these goals. Among the 1,976 Canadian patients in the international Reduction of Atherothrombosis for Continued Health (REACH) Registry, most of whom had established atherosclerotic disease, approximately one quarter were not at their guideline-specified targets for dyslipidemia, one third were not at their targets for fasting blood glucose, and 40% were not at target for blood pressure.[10] Given that these figures are for patients identified as being at high risk through their enrolment in this database, the proportions of patients in the general population with suboptimal control of risk factors are likely to be substantially higher.

Indeed, a retrospective analysis of control of hypertension and dyslipidemia among more than 46,000 patients treated in primary care in southwestern Ontario[11] showed that the rates of control were far worse than among patients in the REACH registry. Overall, the investigators found that only 7% of patients with dyslipidemia but not hypertension achieved guideline-specified targets; 15% of patients with hypertension but not dyslipidemia achieved their targets; and 17% of patients with concomitant dyslipidemia and hypertension achieved both targets.

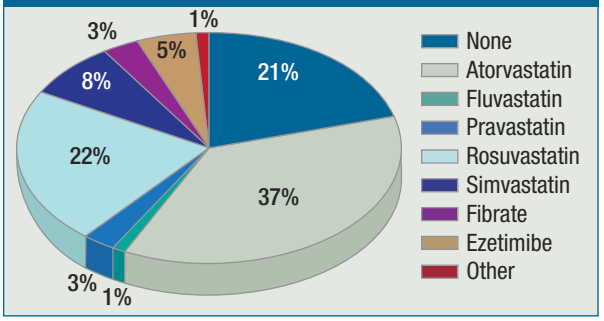
Data are also available from a large practice reflective program, the Assessing Cardiovascular Targets (ACT) program,[12] which involved 676 primary-care physicians across Canada. These participating physicians provided access to chart data for 30 to 40 patients in their practices (total number of patients = 25,489). The program was designed so that physicians could identify patients within their practices who had cardiovascular risks and were already being treated for dyslipidemia with a statin. The goal was to help these physicians better measure their practices—by comparing their practices to guidelines and to their peers nationally—to see how well they were doing in meeting the targets recommended in the 2006 CCS dyslipidemia guidelines.[5] The data were managed and compiled by ISIS Digital Media, an independent health-research firm.

The ACT findings showed that a large proportion of patients in this program were not at the 2006 target levels. Approximately 40.6% had not achieved their goals for LDL-C and 22.2% were not at their targets for blood pressure. The proportions who were not at target for these and other parameters are shown in Table 2. Of the patients with risk level identified (n = 24,033), 57.8% were deemed by their physicians to be at high risk, 24.3% to be at moderate risk and 17.9% to be at low risk. However, independent analysis of risk-factor data showed that

TABLE 2. **Proportions of Patients NOT at Guideline-specified Targets and Proportions of Patients with Other Identified Cardiovascular Risk Factors**[12]

| Target parameter | Proportion of ACT patients NOT at target |
|---|---|
| LDL-C | 40.6% |
| TC:HDL-C ratio | 28.4% |
| Triglycerides | 40.9% |
| Blood pressure | 22.2% |
| Waist circumference | 52.2% |
| **Risk factor** | **Proportion with this risk factor** |
| Metabolic syndrome | 36.8% |
| Fasting blood glucose > 6.2 mmol/L | 34.6% |

FIGURE 1. **Use of Lipid-lowering Medication Among Patients in the ACT Program (n = 24,567)**[12]




45% of patients who were identified by their physicians as being at moderate risk were in fact at high risk (according to Framingham risk score calculations).

With respect to dyslipidemia management, the ACT program also identified the types of agents being used. Of the 24,567 patients with treatment data available, 79% had been prescribed some form of pharmacologic lipid-lowering therapy. The vast majority of these prescriptions were for statin medications. Atorvastatin and rosuvastatin were the most frequently prescribed agents, although older, less potent statins (*i.e.*, simvastatin, pravastatin, fluvastatin) were also represented in this sample (Figure 1).

Overall, the proportions of patients who achieved their LDL-C goals were higher with rosuvastatin or atorvastatin compared to simvastatin, pravastatin or fluvastatin, but even with these more potent agents there were still considerable proportions of patients not at goal. Among patients prescribed atorvastatin, for example, 40% were not at their guideline-specified LDL-C target.

The ACT data were also analyzed to determine the proportions of physicians who initiated or changed treatment based on assessment of their patients' risk factors. Of the 25,490 patients for whom such data were available, 11,625 (46%) had therapy initiated or changed. The types of therapies that were initiated, or to which patients were switched, are shown in Table 3. The two most common therapeutic changes were to switch medication to rosuvastatin or to atorvastatin. These two agents were also the most commonly initiated among these patients.

## Discussion

In the control of cardiovascular risk factors, Canadian physicians have made significant progress in recent years. Control of hypertension, for example, has improved dramatically over the past decade. Data from the Canadian Heart Health Surveys,[13] published in 1997, showed that only 12.2% of patients with hypertension were treated and controlled. A study in Ontario, published in 2008,[14] showed that this proportion had risen to 65.7%. While data such as these are encouraging, research shows that there is still substantial room for improvement and many treatment gaps to bridge. The real-life data compiled in the ACT program show that, for dyslipidemia, approximately four patients in every 10 are not treated to their target levels (based on the 2006 CCS guidelines). It is reasonable to assume that this particular treatment gap would be even wider when examined in the context of the somewhat more aggressive targets recommended in the 2009 guidelines.

There are many potential contributing factors to the dyslipidemia treatment gap. Certainly, ineffective implementation of recommended lifestyle modifications plays a key role,

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as many patients continue to smoke, lead inactive lives and consume inappropriate diets, regardless of the counseling they receive. Underprescription of effective medication also plays a role. In the retrospective study of patients in southwestern Ontario mentioned above,[11] for example, 80% of patients with dyslipidemia were not receiving lipid-lowering therapy. Even among those who are prescribed lipid-lowering therapy, however, the ACT data[12] suggest that there is suboptimal use and modification of available agents. This was illustrated by the fact that many patients in the analysis who were receiving therapy were not at recommended tar-

TABLE 3. **Patients Who Had Therapy Initiated or Changed as a Result of Their Risk Factors: ACT Program Data**[12]

| | Total # of patients with initiation or switch = 11,625 | |
|---|---|---|
| Type of therapy initiation or change | Number of patients with initiation or switch | Percent of patients with initiation or switch |
| Medication changed to rosuvastatin | 1,452 | 12.0% |
| Medication changed to atorvastatin | 1,076 | 9.3% |
| Rosuvastatin initiated | 1,007 | 8.7% |
| Atorvastatin initiated | 458 | 3.9% |
| Rosuvastatin added | 144 | 1.2% |
| Medication changed to simvastatin | 128 | 1.1% |
| Medication changed to pravastatin | 57 | 0.5% |
| Simvastatin initiated | 53 | 0.5% |
| Atorvastatin added | 51 | 0.4% |

gets. The use of less potent statins may have contributed to this treatment gap. Rosuvastatin and atorvastatin are known to be more potent in lowering LDL-C compared to older agents and hence are more likely to result in reaching the targets achieved in the clinical trials. The ACT database shows that the most common strategy employed by physicians who took action based on assessment of their patients' risk factors was to initiate or switch to one of these more potent statins.[12] However, some physicians simply used higher doses of the less potent statins. This approach may achieve LDL-C targets, but at the higher doses of medications the side-effect profile increases as well. Hence, using agents that have higher potency that were used in the recent trials may provide a better risk:benefit ratio for patients.

If even with a good dose of a potent statin the target is still not achieved, then the addition of another agent, such as ezetimibe, niacin or a fibrate may be useful. These combinations have not been tested in terms of hard endpoints such as stroke, myocardial infarction or death, but they do serve a purpose in getting patients' lipid profiles towards targets.

CVD continues to be the leading cause of death and disability in Canada, and its management puts an enormous strain on the Canadian healthcare system. Controlling patients' risk factors to guideline-specified treatment targets can help minimize the impact of CVD. For the vast majority of patients, the tools to achieve these targets already exist (*e.g.*, antihypertensives and lipid-lowering agents). Physicians need to optimize these proven treatment strategies, using potent agents titrated to an effective dose to achieve guideline-specified goals. By achieving these targets, physicians will provide their patients with the benefits of all those clinical trials that have shaped the guidelines. Should these goals not be achievable with optimally dosed statin therapy, then combination therapy can be considered. In the end, by following the guidelines, physicians are essentially following the trials in an attempt to protect their patients from the ravages of CVD.

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