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Position Statement

Identification and Management of Cardiometabolic Risk in Canada: A Position Paper by the Cardiometabolic Risk Working Group (Executive Summary)

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ABSTRACT

With the objectives of clarifying the concepts related to "cardiometabolic risk," "metabolic syndrome" and "risk stratification" and presenting practical strategies to identify and reduce cardiovascular risk in multiethnic patient populations, the Cardiometabolic Working Group presents an executive summary of a detailed analysis and position paper that offers a comprehensive and consolidated approach to the identification and management of cardiometabolic risk. The above concepts overlap and relate to the atherogenic process and development of type 2 diabetes. However, there is confusion about what these terms mean and how they can best be used to improve our understanding of cardiovascular disease treatment and prevention. The concepts related to cardiometabolic risk, pathophysiology, and strategies for identification and management (including health behaviours, pharmacotherapy, and surgery) in the multiethnic Canadian population are presented. "Global cardiometabolic risk" is proposed as an umbrella term for a comprehensive list of existing and emerging factors that predict cardiovascular disease and/or type 2 diabetes. Health behaviour interventions (weight loss, physical activity, diet, smoking cessation) in people identified at high cardiometabolic risk are of critical importance given the emerging crisis of obesity and the consequent epidemic of type 2 diabetes. Vascular protective measures (health behaviours for all patients and pharmacotherapy in appropriate patients) are essential to reduce cardiometabolic risk, and there is growing consensus that a multidisciplinary approach is needed to adequately address cardiometabolic risk factors. Health care professionals must also consider ethnicity-related risk factors in order to appropriately evaluate all individuals in their diverse patient populations.

RÉSUMÉ

Avec l'objectif de clarifier les concepts reliés au ≪ risque cardiométabolique ≫, au ≪ syndrome métabolique ≫ et à la ≪ stratification du risque ≫ et de présenter des stratégies pour identifier et réduire le risque cardiovasculaire chez les populations de patients multiethniques, le groupe de travail sur le métabolisme cardiaque présente un sommaire exécutif d'une analyse fouillée et d'un exposé de principe qui offre une approche complète et consolidée à l'identification et la gestion du risque cardiométabolique. Les concepts ci-dessus s'entrecoupent et s'apparentent au processus et au développement de l'athérogénèse du diabète de type 2. Cependant, il y a confusion sur ce que ces termes signifient et sur la manière de mieux les utiliser pour améliorer notre compréhension du traitement et de la prévention de la maladie cardiovasculaire. Les concepts reliés au risque cardiométabolique et à la pathophysiologie, et les stratégies pour l'identification et la gestion (incluant les comportements de santé, la pharmacothérapie et la chirurgie) dans la population multiethnique canadienne sont présentés. Le ≪ risque cardiométabolique global ≫ est proposé comme terme générique dans une liste exhaustive de nouveaux facteurs et de facteurs existants qui prédisent la maladie cardiovasculaire et/ou le diabète de type 2. Les interventions sur les comportements de santé (perte de poids, activité physique, diète, désaccoutumance du tabac) chez les personnes à risque cardiométabolique élevé sont d'une importance critique étant donné la crise émergente associée à la croissance de l'obésité et les conséquences épidémiques du diabète de type 2. Les mesures de protection vasculaire (les comportements de santé chez tous les patients et la pharmacothérapie chez les patients appropriés) sont essentielles pour réduire le risque cardiométabolique, et il y a un consensus grandissant sur la nécessité d'une approche multidisciplinaire pour répondre adéquatement au risque cardiométabolique. Les professionnels des soins de santé doivent aussi considérer les facteurs de risque liés à l'ethnicité pour évaluer convenablement tous les sujets des diverses populations de patients.

The Cardiometabolic Risk Working Group is a national group of individuals with special interest in cardiometabolic risk and representative of the various related societies. The present article is an executive summary of a position paper[1] written by the Cardiometabolic Risk Working Group to clarify the concepts related to cardiometabolic risk, metabolic syndrome, and cardiovascular risk assessment in a multiethnic Canadian context and to present practical strategies for Canadian physicians to identify and reduce cardiovascular risk in their patients. The full position paper[1] can be found online at http://www.ccs.ca/.

Cardiometabolic Risk, Metabolic Syndrome, and Risk Stratification

The concepts of "cardiometabolic risk" and "metabolic syndrome" and the process of "risk stratification" overlap, and all relate to the atherogenic process and development of type 2 diabetes, an important cardiovascular (CV) risk factor per se. This situation has led to confusion as to what these terms and concepts really mean and how they can best be used to improve our understanding of cardiovascular disease (CVD) treatment and prevention. Accordingly, we offer the following proposals:

1. That the term "cardiometabolic risk" or "global cardiometabolic risk" be considered to represent the comprehensive catalogue of factors that contribute to the development of both CVD and type 2 diabetes. Each of these factors increases the risk of CV morbidity and mortality to some extent, but the term "global cardiometabolic risk" is mainly intended to encourage consideration of factors that go beyond the set of traditional risk factors and that include new or emerging risk factors. The term is intended to be used to catalogue the sources of risk, but not to quantify risk in either absolute or relative terms.
2. That the term "metabolic syndrome" be considered to represent a specific subset of "cardiometabolic risks" that, when clustered together, impart a *relative* increase in risk of CVD and development of type 2 diabetes. Metabolic syndrome has been shown to increase overall lifetime CVD risk[2-5] by about 1.5- to 2-fold.[6,7] Metabolic syndrome has also been shown in some studies to be associated with increased CVD risk independently of its association with dysglycemia and diabetes[2,8-10] and with obesity.[2,11]
3. That the term "risk assessment" or "global risk assessment" be used to describe a process that mathematically weighs the presence or absence of risk factors, as well as their severity, to calculate an *absolute* CV risk by using validated algorithms derived from long-term observational studies in large patient cohorts.

Pathophysiology of Cardiometabolic Risk

The pathophysiological basis of cardiometabolic risk is complex. Although various mechanisms have been proposed, insulin resistance, particularly at the level of the fat, liver, and muscle coupled with visceral/ectopic adiposity and altered adi-

pokine kinetics, appears to be closely associated with the clustering of abnormalities associated with increased cardiometabolic risk—namely dyslipidemia, elevated blood pressure, dysglycemia, and prothrombotic and inflammatory states[12]—that might be the consequence of a complex interplay between various tissues (mainly adipose tissue and liver).

Identification of Cardiometabolic Risk

The goal of screening is to develop, through identification of the significant traditional and nontraditional risk factors, a comprehensive understanding of a patient's risk for cardiometabolic events, thereby enabling appropriate individual preventive measures to be taken. An assessment should occur when any traditional CV risk factor (eg, hypertension or dyslipidemia) is first identified or in patients who are overweight or obese (especially if abdominally obese).[13-20] Screening should include history (including smoking status, family history of premature coronary artery disease or type 2 diabetes, diet, and physical activity level); physical examination (including measurement of blood pressure (BP), waist circumference and body mass index [BMI, calculated as the weight in kilograms divided by height in meters squared]), laboratory tests (including fasting plasma glucose and fasting lipid profile), and other tests (including A1C [glycated hemoglobin], electrocardiogram, exercise stress test, apolipoprotein (apo) B, high-sensitivity C-reactive protein, and renal function) as indicated by patient age, existing risk factors, or guideline-recommended criteria. (See Fig. 1) The calculation of absolute risk by means of a validated algorithm, such as Framingham Risk Score or Reynolds Risk Score, followed by appraisal for the presence or absence of "metabolic syndrome," may help identify patients whose risk might be underestimated through sole consideration of traditional risk factors and who might warrant more comprehensive or intensive intervention, including prompt initiation of health behaviour changes.

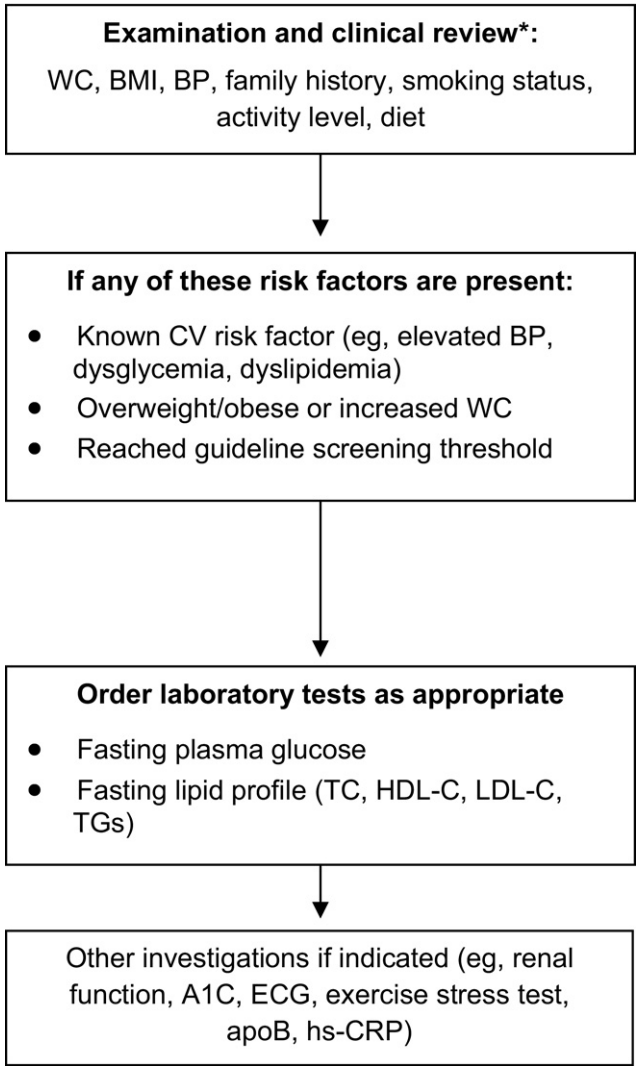

Figure 1. General approach to assessing cardiometabolic risk. A1C, glycated hemoglobin; apoB, apoliprotein B; BMI, body mass index; BP, blood pressure; CV, cardiovascular; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C reactive protein; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TGs, triglycerides; WC, waist circumference.*Annually in those ≥40 years, and opportunistically in those aged 18–39 years.

Interventions to Reduce Cardiometabolic Risk

Health behaviour modification

Health behaviour modification is recommended as the primary treatment strategy for the management of cardiometabolic risk[21-27] and should include simultaneous counselling regarding physical activity, smoking cessation, caloric intake, and diet composition, as these are associated with improvements on all cardiometabolic risk factors. The magnitude of improvement in these variables appears to be dependent on baseline values, with greater improvements reported among those with the greatest disturbances. Although the improvements in cardiometabolic risk factors tend to be more pronounced when a modest reduction in body weight is achieved, significant improvements are also observed even in the absence of significant weight change. These findings support prior recommendations[21,23,24,26] that health behaviour modification, specifically moderate-intensity exercise for 30 to 60 minutes on most days of the week, together with a moderate reduction in caloric intake (~500 kcal/day), can result in significant reductions in cardiometabolic risk. Despite some evidence of a carry-forward effect of short-term health behaviour interventions, the long-term benefit of health behaviour interventions requires sustained efforts in compliance and adherence.

Pharmacologic and surgical interventions

While health behaviour interventions are the primary strategy to reduce cardiometabolic risk, adjunctive pharmacologic therapy or surgery may be required. The majority of pharmacologic interventions to reduce cardiometabolic risk also apply to the patient with diabetes, since most patients with diabetes have increased cardiometabolic risk.[28] There are very few clinical trials that evaluate treatment for individuals with cardiometabolic risk but without either concomitant diabetes or established CVD.

Weight loss. Weight-loss medications (sibutramine or orlistat)

should be used only in association with a weight-reducing diet and increased physical activity.[29] The Sibutramine Cardiovascular Outcomes trial assessed the impact of sibutramine on morbidity and mortality in obese patients with established CVD, diabetes, or both[30] and showed increased CV events in those subjects randomly assigned to sibutramine vs placebo (11.4% of patients vs 10%). Further analyses indicate the increased risk for CV events occurred in patients with a history of CVD, leading the US Food and Drug Administration to contraindicate the use of the drug in patients with a history of CVD. Subsequently, the US Food and Drug Administration concluded that the CV risks posed by sibutramine outweighed the modest weight loss observed with the drug, and asked the manufacturer (Abbott Laboratories) to pull the drug from the market.[31]

For patients with a BMI $\geq$ 30 kg/m^2, or those with a BMI $\geq$ 27 kg/m^2 plus CV risk factors and/or impaired glucose tolerance (IGT), guidelines recommend that weight-loss medications can be considered if weight loss is $<$0.5 kg (1 lb) per week after health behaviour changes have been attempted for 3 to 6 months.[29] There are currently no data to show that weight reduction induced by medications results in improved clinical outcomes. This is in contrast to the reduced event rates consequent to weight reduction resulting from bariatric surgery.[32,33]

Bariatric surgery has been shown to lower all-cause mortality by 24% to 40%[32,33] because of a reduction in deaths from myocardial infarction (MI), diabetes, and cancer, as well as prevention of the development of diabetes in patients with severe obesity.[34] Currently, bariatric surgery can be considered in individuals with class III or above obesity (ie, BMI $\geq$ 40 kg/m^2)[17] or class II obesity (ie, BMI $\geq$ 35 kg/m^2) plus comorbid conditions,[24,35] in whom efforts at medical therapy have failed and who have an acceptable operative risk.

Optimize BP. Clinical trials have not specifically evaluated BP lowering in individuals solely with cardiometabolic risk. However, in patients with cardiometabolic risk associated with dysglycemia, it may be advisable to use agents that may be associated with improvement of glucose metabolism (ie, renin-angiotensin-aldosterone system [RAAS] inhibitors) or antihypertensive drugs that are metabolically neutral (ie, calcium channel blockers [CCBs]). The Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research trial showed that valsartan exerted a modest reduction (14%) in the development of new diabetes in patients with both IGT and heightened CV risk.[36] In the Diabetes Reduction Assessment With Ramipril and Rosiglitazone Medication study, ramipril was found to have a smaller, nonsignificant effect on the prevention of diabetes in individuals with either impaired fasting glucose (IFG) or IGT.[37] In a systematic overview of 3 large trials of angiotensin-converting enzyme (ACE) inhibition in individuals with CVD but without diabetes, a similar reduction in new diagnoses of diabetes was observed.[38] In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial,[39] chlorthalidone treatment was associated with a greater incidence of new diabetes than in patients treated with either amlodipine or lisinopril. Combinations of an ACE inhibitor and CCB compared with therapy that includes a thiazide diuretic are associated with a reduced incidence of new-onset diabetes[40] and improved CV outcomes related to differences in blood glucose level and body weight.[41] In patients with cardiometabolic risk who require BP lowering with multiple agents, the combination of an ACE inhibitor and CCB may be the preferred strategy rather than the combination of an ACE inhibitor and diuretic.[42]

Optimize lipid levels. In patients with cardiometabolic risk with a moderate or high Framingham Risk Score, treatment should be initiated with a statin to reduce low-density lipoprotein cholesterol (LDL-C) by at least 50% and to $<$2.0 mmol/L. Apo B levels are a better measurement of lipid-related risk in these patients, and the target level for treatment is $<$0.8 g/L in high-risk and moderate-risk individuals. There is a large residual risk for patients at high risk for CVD, despite LDL-C reduction with high-dose statins. Many patients with cardiometabolic risk may also have an acquired combined hyperlipidemia, associated with increased triglycerides (TGs), a modest increase in LDL-C, and low high-density lipoprotein cholesterol (HDL-C). LDL particle numbers are increased, as reflected by the increased levels of apo B_{100}. Beyond LDL-C lowering, strategies that might reduce the residual risk include reducing the total cholesterol (TC) to HDL-C ratio, high-sensitivity C-reactive protein, and TG, although there are no clinical trial data to date to support such strategies.[26] In the patient with diabetes, glycemic control optimization and health behaviour modification should be attempted prior to the addition of another agent, such as a fibrate. In the Action to Control Cardiovascular Risk in Diabetes trial[43] the addition of fenofibrate to simvastatin in patients with type 2 diabetes failed to show any reduction of CV events, although there may have been benefit in the subset of individuals with high TG/low HDL-C.

Optimize blood glucose levels, prevent progression to diabetes, and manage hyperglycemia. While health behaviour modification, with weight loss and increased physical activity, is the most effective,[41,44-46] pharmacotherapy can also be considered to prevent progression to type 2 diabetes. Metformin,[44] acarbose,[47] rosiglitazone,[48] pioglitazone,[49] combination therapy with metformin and rosiglitazone,[50] and orlistat[51] have all been shown to reduce progression to type 2 diabetes; however, metformin is indicated as first-line therapy based on its efficacy, safety, and cost. In patients with diabetes, most will require progressively aggressive pharmacotherapy over time with oral antihyperglycemic agents and/or insulin.[25]

Antiplatelet therapy. The benefits of acetylsalicylic acid for primary prevention are very small and offset by the bleeding risks, even when used in patients with risk factors for vascular disease such as diabetes.[52] In the absence of a clinical history of coronary heart disease (MI or angina), stroke, or peripheral arterial disease or of vascular imaging showing atherosclerosis, there is no evidence to support the use of acetylsalicylic acid in patients with cardiometabolic risk.

Smoking cessation. In addition to counselling, medications (nicotine replacement, buproprion, or varenicline) should be offered to most patients who are motivated to stop smoking.

Cardiometabolic Risk in Susceptible Canadian Populations

How do ethnicity and culture impact on cardiometabolic risk?

Canada is one of the world's most ethnically diverse countries, and CVD rates vary considerably among Canadians of different ethnic origins.[53] The reasons for this variation have not been fully elucidated[54] but suggest that studies carried out in European populations cannot be fully extrapolated to other ethnocultural populations.[53] In addition, as the relationship between percentage body fat and BMI varies by ethnic population, ethnic-specific thresholds for the definition of overweight[55] and central adiposity[56] are recommended. Despite differences among populations, it is important to note that collectively, the following 9 risk factors account for 90% of the population-attributable risk of MI in men and 94% in women: abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial stress, lack of consumption of fruits and vegetables, lack of moderate alcohol consumption, and physical inactivity.[57]

Traditional risk factors explain the majority of CV events in all populations.[57] Thus, health behaviours and pharmacologic interventions to reduce cardiometabolic risk should be optimally applied to all patient populations as per national guidelines and as per the suggestions outlined earlier in this document. Whether specific ethnic groups would benefit from therapies different from those recommended in guidelines or from differential treatment targets remains unclear. However, it is widely known that certain groups, such as blacks, may have a reduced BP-lowering response to RAAS blockers, and thus these agents may not be ideal as first-line drugs for the management of hypertension.[39] Similarly, antihypertensive agents that improve glucose metabolism (ie, RAAS inhibitors) or that are metabolically neutral (ie, CCBs) may be preferable as first-line therapy in populations prone to diabetes, such as South Asians. Differences in statin efficacy between ethnic groups may be attributable to differences in pharmacokinetic and pharmacodynamic effects or to polymorphisms of genes critical to drug metabolism.[58] Asians have historically been considered to be more responsive to the lipid-lowering effects of statins than are white populations. As such, Health Canada and the US Food and Drug Administration recommend lower starting doses of certain statins in Asian patients.[59,60] Recent data, however, suggest that people of South Asian origin and white populations derive similar lipid effects from atorvastatin and simvastatin and that dose adjustment in South Asians may not be necessary.[61] As the cultural dynamics of chronic illnesses and their management are complex and often deeply rooted in cultural traditions, community-based prevention and management programs should be developed and delivered in partnership with target communities.

Conclusion

"Global cardiometabolic risk" is an umbrella term for a comprehensive list of existing and emerging factors that predict CVD and/or type 2 diabetes. Health behaviour interventions in people identified at high cardiometabolic risk are of critical importance given the emerging crisis of obesity in Westernized countries and the consequent epidemic of type 2 diabetes.[12,13,15,62-64] Vascular protective measures are essential for all patients with cardiometabolic risk, and there is growing consensus that a multidisciplinary approach[24,25] is needed to adequately address cardiometabolic risk factors. Family physicians play a key role in identifying people with increased cardiometabolic risk but often do not have the time or resources to deliver evidence-based, cost-effective interventions that promote sustainable health behaviour change among their patients. Primary health care reform offers opportunities for inclusion of exercise specialists (kinesiologists) and nutrition specialists (registered dietitians) in primary health care teams. Finally, Canadian health care professionals must also consider ethnicity-related risk factors in order to appropriately evaluate all individuals in their diverse patient populations.

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Supporting Organizations

C-CHANGE, Canadian Cardiovascular Society, Canadian Diabetes Association, Canadian Institutes of Health Research, Canadian Obesity Network, The College of Family Physicians Canada, Dietitians of Canada, Obesity Canada.

References

1. Leiter LA, Fitchett DH, Gilbert RE, et al; for the Cardiometabolic Risk Working Group. Cardiometabolic risk in Canada: a detailed analysis and position paper by the Cardiometabolic Risk Working Group. Can J Cardiol 2011; 27: e1-e33.
2. Daly CA, Hildebrandt P, Bertrand M, et al; for the EUROPA investigators. Adverse prognosis associated with the metabolic syndrome in established coronary artery disease: data from the EUROPA trial. Heart 2007; 93:1406-11.
3. Mellen PB, Cefalu WT, Herrington DM. Diabetes, the metabolic syndrome, and angiographic progression of coronary arterial disease in postmenopausal women. Arterioscler Thromb Vasc Biol 2006;26:189-93.
4. Nilsson PM, Engström G, Hedblad B. The metabolic syndrome and incidence of cardiovascular disease in non-diabetic subjects: a population-based study comparing three different definitions. Diabet Med 2007;24: 464-72.
5. Nilsson PM. Cardiovascular risk in the metabolic syndrome: fact or fiction? Curr Cardiol Rep 2007;9:479-85.
6. Galassi A, Reynolds K, He J. Metabolic syndrome and the risk of cardiovascular disease: a meta-analysis. Am J Med 2006;119:812-9.
7. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol 2007;49:403-14.

8. Noto D, Barbagallo CM, Cefalù AB, et al. The metabolic syndrome predicts cardiovascular events in subjects with normal fasting glucose: results of a 15 years follow-up in a Mediterranean population. Atherosclerosis 2008;197:147-53.

9. Lorenzo C, Williams K, Hunt KJ, Haffner SM. The National Cholesterol Education Program–Adult Treatment Panel III, International Diabetes Federation, and World Health Organization definitions of the metabolic syndrome as predictors of incident cardiovascular disease and diabetes. Diabetes Care 2007;30:8-13.

10. de Simone G, Devereux RB, Chinali M, et al; for the Strong Heart Study Investigators. Prognostic impact of metabolic syndrome by different definitions in a population with high prevalence of obesity and diabetes: the Strong Heart Study. Diabetes Care 2007;30:1851-6.

11. Arnlov J, Ingelsson E, Sundstrom J, Lind L. Impact of body mass index and the metabolic syndrome on the risk of cardiovascular disease and death in middle-aged men. Circulation 2010;121:230-6.

12. Després J-P, Lemieux I, Bergeron J, et al. Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. Arterioscler Thromb Vasc Biol 2008;28:1039-49.

13. Mente A, Yusuf S, Islam S, et al. Metabolic syndrome and risk of acute myocardial infarction: a case-control study of 26 903 subjects from 52 countries. J Am Coll Cardiol 2010;55:2390-8.

14. Després J-P, Tchernof A. Classification of overweight and obesity. In: 2006 Canadian clinical practice guidelines on management and prevention of obesity in adults and children. CMAJ 2007;176:Online-21-6. Available at: http://www.cmaj.ca/cgi/data/176/8/S1/DC1/1. Accessed January 20, 2011.

15. Després J-P, Cartier A, Côté M, Arsenault BJ. The concept of cardiometabolic risk: bridging the fields of diabetology and cardiology. Ann Med 2008;40:514-23.

16. Mathieu P, Pibarot P, Larose E, Poirier P, Marette A, Després J-P. Visceral obesity and the heart. Int J Biochem Cell Biol 2008;40:821-36.

17. Poirier P, Alpert MA, Fleisher LA, et al. Cardiovascular evaluation and management of severely obese patients undergoing surgery: a science advisory from the American Heart Association. Circulation 2009;120:86-95.

18. Poirier P, Eckel RH. Cardiovascular consequences of obesity. Drug Discov Today: Ther Strategies 2008;5:45-51.

19. Poirier P, Lemieux I, Mauriège P, et al. Impact of waist circumference on the relationship between blood pressure and insulin. The Quebec Health Survey. Hypertension 2005;45:363-7.

20. Poirier P. Healthy lifestyle: even if you are doing everything right, extra weight carries an excess risk of acute coronary events. Circulation 2008; 117:3057-9.

21. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome: a new world-wide definition: a consensus statement from the International Diabetes Federation. Diabet Med 2006;23:469-80.

22. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C; American Heart Association; National Heart, Lung, and Blood Institute. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004;109:433-8.

23. Grundy SM, Hansen B, Smith SC Jr, Cleeman JI, Kahn RA; American Heart Association; National Heart, Lung, and Blood Institute. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. Circulation 2004;109:551-6.

24. Lau DC, Douketis JD, Morrison KM, et al. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. CMAJ 2007;176:S1-13.

25. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Clinical practice guidelines for the prevention and management of diabetes in Canada. Can J Diabetes 2008;32(suppl 1):S1-201.

26. Genest J, McPherson R, Frohlich J, et al. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult – 2009 recommendations. Can J Cardiol 2009;25:567-79.

27. Canadian Hypertension Education Program. Recommendations 2010. Available at: http://hypertension.ca/chep/recommendations-2010/. Accessed September 13, 2010.

28. Alexander CM, Landsman PB, Teutsch SM, Haffner SM; Third National Health and Nutrition Examination Survey (NHAMES III), National Cholesterol Education Program (NCEP). NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. Diabetes 2003;52: 1210-4.

29. Sharma AM, Douketis JD. Pharmacotherapy for obesity: adults. In: 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children. CMAJ 2007;176:online 66-71. Available at: http://www.cmaj.ca/cgi/data/176/8/S1/DC1/1. Accessed January 20, 2011.

30. James WPT, Caterson ID, Coutinho W, et al. Effect of sibutramine on cardiovascular outcomes in overweight and obese subjects. N Engl J Med 2010;363:905-17.

31. US Food and Drug Administration. Follow-up to the November 2009 early communication about an ongoing safety review of sibutramine, marketed as Meridia. Available at: www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm198206.htm. Accessed September 13, 2010.

32. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. N Engl J Med 2007;357:753-61.

33. Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med 2007;357:741-52.

34. Sjöström L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004;351,2683-93.

35. Mechanick JI, Kushner RF, Sugerman HJ, et al. American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient. Endocr Pract 2008;14(suppl 1):1-83.

36. Holman R, Haffner S, McMurray JJ, et al. Effect of nateglinide on the incidence of diabetes and cardiovascular events. N Engl J Med 2010;362: 1463-76.

37. DREAM Trial Investigators. Effects of ramipril and rosiglitazone on cardiovascular and renal outcomes in people with impaired glucose tolerance or impaired fasting glucose: results of the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) trial. Diabetes Care 2008;31:1007-14.

38. Dagenais GR, Pogue J, Fox K, Simoons ML, Yusuf S. Angiotensin-converting-enzyme inhibitors in stable vascular disease without left ventricular systolic dysfunction or heart failure: a combined analysis of three trials. Lancet 2006;368:581-8.

39. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288:2981-97.

40. Bakris G, Molitch M, Hewkin A, et al. Differences in glucose tolerance between fixed-dose antihypertensive drug combinations in people with metabolic syndrome. Diabetes Care 2006;29:2592-7.

41. Poulter NR, Wedel H, Dahlöf B, et al. Role of blood pressure and other variables in the differential cardiovascular event rates noted in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA). Lancet 2005;366:907-13.

42. Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. N Engl J Med 2008;359:2417-28.

43. ACCORD Investigators. Effects of combination lipid therapy in type 2 diabetes mellitus. N Eng J Med 2010;362:1563-74.

44. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.

45. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343-50.

46. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. Diabetes Care 1997;20:537-44.

47. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M. Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial. JAMA 2003;290:486-94.

48. DREAM Trial Investigators. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet 2006;368:1096-105.

49. DeFronzo R. ACTos NOW for the prevention of diabetes (ACT NOW) study. Oral presentation at: American Diabetes Association 68th Scientific Sessions. June 9, 2008, San Francisco, CA.

50. Zinman B, Harris SB, Neuman J, et al. Low-dose combination therapy with rosiglitazone and metformin to prevent type 2 diabetes mellitus (CANOE trial): a double-blind randomised controlled study. Lancet 2010; 376:103-11.

51. Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomised study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care 2004;27:155-61.

52. Berger JS, Roncaglioni MC, Avanzini F, Pangrazzi I, Tognoni G, Brown DL. Aspirin for the primary prevention of cardiovascular events in women and men: a sex-specific meta-analysis of randomized controlled trials. JAMA 2006;295:306-13.

53. Anand SS, Yusuf S, Vuksan V, et al; for the SHARE Investigators. Differences in risk factors, atherosclerosis, and cardiovascular disease between ethnic groups in Canada: the Study of Health Assessment and Risk in Ethnic groups (SHARE). Lancet 2000;356:279-84.

54. Liu J, Hanley AJ, Young TK, Harris SB, Zinman B. Characteristics and prevalence of the metabolic syndrome among three ethnic groups in Canada. Int J Obes (Lond) 2006;30:669-76.

55. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363(9403):157-63.

56. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640-5.

57. Yusuf S, Hawken S, Ounpuu S, et al; for the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004;364:937-52.

58. Liao JK. Safety and efficacy of statins in Asians. Am J Cardiol 2007;99: 410-14.

59. Health Canada. Association of CRESTOR (rosuvastatin) with muscle-related adverse events – AstraZeneca Inc. Available at: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/public/_2005/crestor_2_pa-ap-eng.php. Accessed September 13, 2010.

60. FDA Public Health Advisory on Crestor (rosuvastatin). Available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/PublicHealthAdvisories/ucm051756.htm. Accessed February 25, 2011.

61. Gupta M, Braga MF, Teoh H, Tsigoulis M, Verma S. Statin effects on LDL and HDL cholesterol in South Asian and white populations. J Clin Pharmacol 2009;49:831-7.

62. Sattar N, McConnachie A, Shaper AG, et al. Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. Lancet 2008;371:1927-35.

63. Sattar N. The metabolic syndrome: should current criteria influence clinical practice? Curr Opin Lipidol 2006;17:404-11.

64. American Diabetes Association. Understanding Cardiometabolic Risk: Broadening Risk Assessment and Management. Alexandria, VA: American Diabetes Association; 2007.