Position Statement

Cardiometabolic Risk in Canada: A Detailed Analysis and Position Paper by the Cardiometabolic Risk Working Group

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ABSTRACT

The concepts of “cardiometabolic risk,” “metabolic syndrome,” and “risk stratification” overlap and relate to the atherogenic process and development of type 2 diabetes. 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. With the

RÉSUMÉ

Les concepts de « risque cardiométabolique », de « syndrome métabolique » et de « stratification du risque » s’entrecoupent et s’apparentent au processus et au développement de l’athérogénèse du diabète de type 2. 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

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See page e24 for disclosure information.
In cases in which guidelines did not exist, literature searches evidence-based guidelines were used to inform this position paper. An executive summary of the position paper was also developed to highlight key messages. Recommendations for the identification and management of cardiovascular (CV) risk factors are summarized. An executive summary of the evidence surrounding emerging risk factors not captured in traditional risk engines, key literature and existing guideline recommendations for the 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 risk factors related to ethnicity in order to appropriately evaluate everyone in their diverse patient populations.

The Cardiometabolic Risk Working Group is a national group of individuals with special interest in cardiometabolic risk and representative of the various related societies. In 2009, the Cardiometabolic Risk Working Group conceptualized the idea of organizing a consensus meeting that would be coupled with the publication of a position paper conceived with Canadian expertise and with direct and practical relevance for the diverse Canadian population and Canadian clinicians. In addition to providing readers with an introduction to the concept of cardiometabolic risk and the evidence surrounding emerging risk factors not captured in traditional risk engines, key literature and existing guideline recommendations for the identification and management of cardiovascular (CV) risk factors are summarized. An executive summary of the position paper was also developed to highlight key messages in an abbreviated format.

To consolidate relevant approaches, existing Canadian evidence-based guidelines were used to inform this position paper. In cases in which guidelines did not exist, literature searches were performed to locate high-quality primary studies and review articles. In addition, personal files and reference lists were searched for relevant studies. Formal searches were restricted to human studies published in the English-language literature from 2004 onwards and listed in PubMed, EMBASE, and the Cochrane Library. A close-to-final version of the document was reviewed by representatives of supporting organizations.

**Objectives and Methods**

The Cardiometabolic Risk Working Group is a national group of individuals with special interest in cardiometabolic risk and representative of the various related societies. In 2009, the Cardiometabolic Risk Working Group conceptualized the idea of organizing a consensus meeting that would be coupled with the publication of a position paper conceived with Canadian expertise and with direct and practical relevance for the diverse Canadian population and Canadian clinicians. In addition to providing readers with an introduction to the concept of cardiometabolic risk and the evidence surrounding emerging risk factors not captured in traditional risk engines, key literature and existing guideline recommendations for the identification and management of cardiovascular (CV) risk factors are summarized. An executive summary of the position paper was also developed to highlight key messages in an abbreviated format.

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**Introduction to the Concepts of Cardiometabolic Risk, Metabolic Syndrome, and Risk Stratification: Finding the Forest Among the Trees**

Atherogenesis is a complicated process. A panoply of mechanisms are at play, all of which are influenced by multiple factors, such as genetic predisposition or susceptibility, dyslipidemia, and oxidant state. Similarly, the genesis of type 2 diabetes is a complicated process. While many of the features and processes involved in the development of this disease overlap

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with the factors affecting atherosclerosis, others are distinct. The fact that type 2 diabetes is often complicated by atherosclerosis further complicates the interplay of processes affecting one or the other or both conditions. Bench research continues to create an ever more comprehensive and detailed understanding of atherogenesis and diabetes, but translation of this information into the clinical arena is difficult. It is dependent on how important a particular pathway might be in causing clinical disease, how well we can gauge such underlying processes, and whether we can actually offer treatments. For example, it is relatively easy to measure and treat blood pressure (BP) and to measure and treat lipid status. However, it is not easy, and perhaps not even currently important, to assess factors that may be implicated in both atherogenesis and development of type 2 diabetes but for which there are no specific or proven therapies.

The objective of this broad introduction is to put into context the purpose and value of the concepts of “cardiometabolic risk” and “metabolic syndrome” and the process of “risk stratification.” All these concepts overlap, and all relate to the atherogenic process, as well as the resultant morbidity and mortality. Additionally, in response to secular trends in the frequency of obesity and diabetes, the terms are intimately linked to the risk for development of type 2 diabetes, an important CV risk factor per se. This situation has led to confusion about 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 both CVD and development of 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 novel or emerging risk factors. The term is intended 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 be a specific subset of cardiometabolic risks. This subset of factors has been the focus of numerous studies that have demonstrated that when they are clustered together, they impart a relative increase in risk of CVD and development of type 2 diabetes.

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 using validated algorithms derived from long-term observational studies in large patient cohorts.

What is meant by cardiometabolic risk?

The term “cardiometabolic risk” was first employed by the American Diabetes Association as an umbrella term to include all the risk factors for diabetes and CVD. The term was generated to acknowledge that a circumscribed focus on the clustering of risk factors known as metabolic syndrome (see below) was not an optimal strategy for determining individual risk for diabetes and CVD. Rather, it was suggested that clinicians should evaluate and treat all CVD risk factors. A definition of the term “global cardiometabolic risk” and its application in clinical practice was also described by Despres and Lemieux in 2006. They also encompassed traditional risk factors, as well as more novel or emerging risk factors (eg, prothrombotic profile, inflammatory state; see Fig. 1). Thus, a main goal of this concept or approach is to emphasize everything known clinically to affect CVD, including the emergence of type 2 diabetes, in a fashion analogous to the bench researcher’s goal of accounting for all known mechanisms when studying the atherosclerotic process. Thus, the notion of “global” risk assessment, meaning “comprehensive” risk assessment, is implied by those who use the term “cardiometabolic risk” or “global cardiometabolic risk.” Even so, the term “global” is perhaps not comprehensive enough insofar as its main genesis was to amalgamate risks for both coronary diseases with those for the development of type 2 diabetes. One might argue, for example, that both the postmenopausal state in women and the presence of erectile dysfunction in men are cardiometabolic risks for atherosclerosis and associated morbidity and mortality, but they are not generally included in discussions of global cardiometabolic risk. Even so, if one accepts the value of the concept as an all-encompassing term, then the term becomes broad enough to envelop both established and emerging risk factors. And one should anticipate that the catalogue of factors contributing to global cardiometabolic risk will continue to expand as research continues.

What is meant by metabolic syndrome?

The central tenet of the global cardiometabolic risk concept is that it captures the risk of CVD and type 2 diabetes (see Fig. 1). Metabolic syndrome also does this to some degree, but it encompasses a more limited cluster of metabolic abnormalities linked to insulin resistance, which is often associated with abdominal obesity, the high-risk form of overweight and obesity. This more circumscribed set of clinical parameters describes a constellation of features originally known as “syndrome X.” This pattern recognition process was linked together mechanistically by emphasizing insulin resistance or hyperinsulinemia in association with excessive visceral and ectopic fat deposition and manifested by sometimes subtle abnormalities of blood glucose, BP, triglycerides (TGs), and/or low high-density lipoprotein cholesterol (HDL-C). The underlying mechanism leading to this clustering of features appears more complicated than merely insulin resistance or hyperinsulinemia and is now felt to encompass both prothrombotic and proinflammatory mechanisms as well. (See the section titled Pathophysiology of Cardiometabolic Risk.) In spite of the uncertainty regarding the precise reason for clustering of features of metabolic syndrome, the clinical reality is that this constellation is a common and important determinant of the development of both cardiac disease and diabetes.

The intense research interest in this specific constellation of findings has prompted attempts to define the syndrome explicitly. The diversity of criteria for metabolic syndrome has contributed to confusion pertaining to this concept. In many respects, the concept is an exercise in the counting of risk factors, some of which are “classical” and some of which are more novel (eg, waist circumference). Moreover, the risk factors may be present at subtle levels (eg, impaired fasting
glucose [IFG]) or at levels that define a disease state (eg, type 2 diabetes or “treated diabetes” or “treated hypertension”). However, excluding the early World Health Organization criteria that included consideration of renal dysfunction,9 there has emerged a general consensus that the key features of metabolic syndrome include visceral obesity, dysglycemia, BP abnormalities, elevated TGs, and low HDL-C.10-12 The variance in the definitions proposed by different groups pertains mainly to the thresholds used to designate presence or absence of a given feature in a specific patient of a specific ethnic background (see Table 1). While it is important to keep these differences in mind when evaluating any given publication in this arena, it is perhaps more important to emphasize that it is generally accepted that metabolic syndrome increases overall lifetime CVD risk13-16 about 1.5- to 2-fold.17,18 It has also been shown in some studies to be associated with increased CVD risk independently of its association with dysglycemia and diabetes13,19-21 and with obesity.13,22

Recently, a harmonized set of criteria was agreed on by the International Diabetes Federation Task Force on Epidemiology and Prevention, the National Heart, Lung and Blood Institute, the American Heart Association, the World Heart Federation, the International Atherosclerosis Society, and the International Association for the Study of Obesity (see Table 1).23 Although high waist circumference was a prerequisite for defining the syndrome, as in the older International Diabetes Federation criteria,12 it is not a requirement of the harmonized definition. An analysis by Arnlov and colleagues22 appears to justify this shift, at least with respect to risk of CVD and mortality in middle-aged men, but perhaps it renders the clustering less useful for the prediction of diabetes. At any rate, the syndrome is currently based on the presence of at least 3 abnormal values out of 5 criteria (waist circumference, BP, fasting plasma glucose [FPG], HDL-C, and TGs), without regard for severity or duration. Thus, while this yes-or-no, or dichotomous, assessment of the presence or absence of features identifies the syndrome, and while the presence of this syndrome imparts a higher relative risk of both CVD and diabetes, the assessment is not designed to establish an absolute risk and should not be used for this purpose. Determining the absence or presence of metabolic syndrome does, however, ensure that the component risk factors are assessed in clinical practice, allowing the clinician to see the “big picture” and to recognize a pattern from a variety of risk factor measures.15,16,24 Perhaps the most important contribution is that it allows one to consider these cardiometabolic risk factors irrespective of whether they are yet severe.

**How are metabolic syndrome and risk assessment algorithms used to predict individual CVD risk?**

The assessment of absolute risk requires validated, mathematical algorithms such as the Framingham Risk Score (FRS) or others. These algorithms include some of the factors that are a part of the assessment required to determine presence of metabolic syndrome, but not all of them. For example, the FRS does not incorporate waist circumference or TG level, whereas assessment of these factors is essential in attempting to identify the presence of metabolic syn-
The syndrome is certainly not sufficient to quantify risk in absolute terms. The presence of metabolic syndrome leads to a 1.5- to 2-fold increase in relative CVD risk. Accordingly, consideration of this syndrome may help to identify patients in whom available risk algorithms may underestimate true risk.

The difference and interdigitation between the 2 approaches can be illustrated by several simple considerations. For example, let us consider a patient with systolic BP of 135 mm Hg, an HDL-C of 0.9 mmol/L, and a TG of 1.8 mmol/L, who, by virtue of fulfilling 3 of the 5 criteria, can be said to have metabolic syndrome. Such a patient is perceived to have a relative 1.5- to 2-fold increase of CV risk. But what is the absolute
CV risk to begin with? In order to calculate absolute risk, we need a validated algorithm. Irrespective of the algorithm selected, all of them would yield a higher absolute risk for a man than for a woman for the identical constellation of findings noted above. Similarly, all else being equal, a younger patient of either gender will have a lower absolute risk than will an older patient of the same gender. Of the algorithms available, only the Prospective Cardiovascular Munster Study algorithm would have incorporated a factor weighing TGs, an element of the patient profile also required to assess presence or absence of metabolic syndrome. In contrast, the algorithms more commonly used in North America (FRS and Reynolds Risk algorithms) would not incorporate the impact of a TG abnormality.

The individual described in the clinical case above does not have abdominal obesity. Consider, therefore, a case with completely normal TGs but with the same BP and HDL-C, as well as a high waist circumference (specific to gender and ethnic background – see Table 1). None of the formal algorithms take waist circumference into account. Accordingly, the implication is that whatever absolute risk is computed by the chosen algorithm, the presence of the constellation of findings confirming presence of metabolic syndrome would cause one to reconsider or to question the calculated absolute risk and perhaps to readjust it higher by a relative factor of about 1.5 to 2. While this implication is not fully accepted or fully validated, the practical importance is likely to be most critical in patients who might be considered to have only low or moderate risk by the traditional risk assessment algorithms. Figure 2 shows an example that illustrates this issue.

Thus, in clinical practice, it is prudent to first calculate an absolute CV risk using a well-validated algorithm. To more fully capture the global cardiometabolic risk, and hence the possibility of additional CVD risk, the construct of metabolic syndrome should be weighed if the patient fulfills those criteria. Given the emerging crisis of obesity in Westernized countries and the consequent epidemic of type 2 diabetes, the concept of cardiometabolic risk serves mainly to allow practitioners to recognize early stages of CVD risk from a more comprehensive list of factors than represented in risk-calculation algorithms and that, in concert, warrant therapeutic health behaviour changes designed to promote weight loss.

Although the current consensus definition does not require elevated waist circumference to be present to identify metabolic syndrome, the importance of obesity, particularly abdominal obesity and the potential importance of hyperinsulinemia in many of these patients, still deserves major consideration (see the Pathophysiology of Cardiometabolic Risk section below).

What are the limitations of current approaches to assessing CVD risk?

Després and colleagues have outlined the advantages and disadvantages of the cardiometabolic risk concept in the context of risk assessment using traditional factors (see Table 2). The concept of a metabolic “syndrome” is controversial, and its application in clinical practice has proven to be problematic. The prevalence of metabolic syndrome within individual cohorts varies with the definition used, and within each definition it increases with age and varies with gender and ethnicity. It is unclear whether each definition is equally predictive of CVD, whether all possible combinations of risk factors within each definition are equally predictive, and whether the presence of the clinical criteria for metabolic syndrome truly increases the risk of CVD beyond traditional risk factors. Furthermore, meeting the clinical criteria for metabolic syndrome does not necessarily confer a very high absolute risk of CVD, as illustrated in the clinical example above and in Figure 2. Also, in a population-based cohort study comparing prevalence rates and the prediction of CVD using different definitions of metabolic syndrome, single risk factors such as smoking had a predictive ability equal to that of metabolic syndrome. Differing definitions have been shown to be associated with measures of subclinical carotid atherosclerosis, but the associations were entirely mediated by the individual criteria of metabolic syndrome. Consequently, the diagnosis of metabolic syndrome (irrespective of the definition chosen) may not provide any additional information beyond the component risk factors with respect to subclinical atherosclerosis, suggesting that the CV risk associated with metabolic syndrome is derived mainly from its key components, namely, abdominal obesity, BP, and blood glucose.
As discussed earlier, metabolic risk factor criteria are dichotomous (either you meet the criteria or you don’t) and as such do not reflect the continuous nature of risk. Thus, various individuals with borderline and elevated risk factors could all be said to have metabolic syndrome, but each individual’s risk would be very different.

But formal risk-assessment algorithms are also not without problems. Different risk-assessment methods sometimes lead to differences in risk estimates. While these may be useful tools for evaluating an individual’s coronary artery disease (CAD) risk, several limitations need to be considered:

- The prediction model may not be similarly applicable to all populations.
- Risk prediction algorithms may not be equally predictive in men and women.
- These assessment methods may not be equally predictive for people with type 2 diabetes.
- There may be differences in the CVD and CAD endpoints considered.
- The risk prediction models may consider only a limited number of risk factors or markers. A number of other factors that appear to predict risk and/or refine risk stratification are not always included, eg, subclinical atherosclerosis, apolipoprotein (apo) B, apo B-to-AI ratio, high-sensitivity C-reactive protein (hs-CRP), LP(a), coronary artery calcification score, ankle-brachial index, carotid plaque, carotid atherosclerosis, carotid artery intima-media thickness, A1C (glycated hemoglobin), lipoprotein-associated phospholipase A2, abdominal obesity, health behaviour risk factors (lack of fruit and vegetable intake, lack of regular exercise, and lack of mild to moderate alcohol consumption), and brain natriuretic peptide (or N-terminal prohormone brain natriuretic peptide). Identification and weighting of these factors may allow more precise risk stratification and perhaps earlier diagnosis and intervention in patients at risk for or with occult CVD.
- Most equations do not optimally assess lifetime risk.
- Risk assessment methods are not applicable to children and adolescents.
- Socioeconomic status may be an important confounder in the association of metabolic syndrome with CAD risk.
- They may predict risk but not progression of atherosclerosis.
- Although risk factors such as age, cholesterol, and BP are included as continuous variables in the various risk assessment algorithms, other risk factors, such as smoking, diabetes, and, for some risk engines, family history, are considered only as dichotomous variables (present or absent), although extensive data suggest that the relationship of these risk factors to CVD risk is more complex and dependent not only on the presence or absence of these risk factors but also on quantitative exposure to the respective risk factor.
- Classical CVD risk assessment algorithms focus on the relatively short-term horizon (5 to 10 years), whereas lifelong risk may be more relevant, especially in terms of primary prevention.
- There is controversy about “biochemical” risk factors and subclinical atherosclerosis (coronary artery calcium, carotid artery intima-media thickness, and carotid plaque). Subclinical atherosclerosis is not a risk factor but rather a structural change of the vascular wall in response to the long-term exposure to various risk factors modulated by genetically determined response (susceptibility) of the individual; many would consider subclinical atherosclerosis as evidence of vascular disease and not a CVD risk factor.

**Summary**

We have attempted to clarify several terms and processes that overlap and cause confusion. We propose that “global cardiometabolic risk” is an umbrella term for a comprehensive list of existing and emerging factors that predict CVD and/or type 2 diabetes, and we furthermore suggest that this catalogue of factors will continue to expand. Secondly, we highlight that the term “metabolic syndrome” pertains to a subset of this comprehensive list for which explicit criteria have been proposed. These criteria help to provide some clarity for ongoing studies and interpretation of the explosion of research reports pertaining to metabolic syndrome. And of practical clinical importance, patients who meet criteria for metabolic syndrome appear to have a relative increase in CV risk by a factor of about 1.5 to 2. We stress, however, that the components of the definition of metabolic syndrome may not be equally weighted in terms of leading to the increased relative CV risk. Furthermore, we narrowly limit the concept of absolute risk assessment as a process requiring the use of validated algorithms derived from large cohorts of patients followed for long periods of time. Finally, we suggest that the calculation of an absolute risk fol-
Pathophysiology of Cardiometabolic Risk
S. Verma, R.E. Gilbert, R. Rabasa-Lhoret, and H. Teoh

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 adiposity, and altered adipokine kinetics, appear to be closely associated with the clustering of abnormalities associated with increased cardiometabolic risk.

What is the contribution of visceral adiposity to cardiometabolic risk?

The association between increased visceral/ectopic adiposity and insulin resistance has been demonstrated by Després and colleagues (see Fig. 3). The hyperlipolytic and insulin-resistant state of the omental adipose tissue exposes the liver to high concentrations of FFAs. This in turn impairs several hepatic metabolic processes, leading to hyperinsulinemia (via increased hepatic glucose production), glucose intolerance (via increased insulin clearance), and hypertriglyceridemia (via increased VLDL–apolipoprotein B secretion). The visceral adipose tissue serves as a powerful source of local and systemic inflammatory molecules—cytokines and adipokines that potentiate tissue insulin resistance and also cause systemic endothelial injury and promote atherosclerosis. Excessive visceral fat accumulation is also associated with ectopic fat deposition in undesired sites such as the liver, the heart, the skeletal muscle, and the pancreas, further contributing to the metabolic abnormalities that increase risk for CVD and type 2 diabetes. Adapted and reproduced with permission from Després JP, Lemieux I, Bergeron J, et al.4 FFA, free fatty acid; IL-6, interleukin-6; TG, triglyceride; TNF-α, tumour necrosis factor-α; VLDL, very low-density lipoprotein.

What is the contribution of visceral adiposity to cardiometabolic risk?

In order to maintain normoglycemia, hyperinsulinemia develops in response to insulin resistance. Insulin regulates over 700 genes, so the implications of hyperinsulinemia are significant and far reaching. While the direct contribution of insulin resistance to global cardiometabolic risk is the subject of

Lowed by a reappraisal based on the presence or absence of metabolic syndrome may help to identify patients whose risk may be underestimated through sole consideration of traditional risk factors and who may warrant more comprehensive or more intensive intervention, including prompt initiation of health behaviour changes (see Health Behaviour Interventions below). The latter is of critical importance given the emerging crisis of obesity in Westernized countries and the consequent epidemic of type 2 diabetes.6,30,59-62

Figure 3. Proposed mechanisms by which visceral obesity could be linked to the atherothrombotic-inflammatory abnormalities of insulin resistance. (A) The hyperlipolytic and insulin-resistant state of the omental adipose tissue exposes the liver to high concentrations of FFAs. This in turn impairs several hepatic metabolic processes, leading to hyperinsulinemia (via decreased insulin clearance), glucose intolerance (via increased hepatic glucose production), and hypertriglyceridemia (via increased VLDL–apolipoprotein B secretion). (B) The visceral adipose tissue serves as a powerful source of local and systemic inflammatory molecules—cytokines and adipokines that potentiate tissue insulin resistance and also cause systemic endothelial injury and promote atherosclerosis. (C) Excessive visceral fat accumulation is also associated with ectopic fat deposition in undesired sites such as the liver, the heart, the skeletal muscle, and the pancreas, further contributing to the metabolic abnormalities that increase risk for CVD and type 2 diabetes.4,59

VISCERAL OBESITY = DYSFUNCTIONAL ADIPOSE TISSUE?

- Insulin resistance
  - Portal circulation
  - Altered FFA metabolism
  - Hyperinsulinemia
  - Glucose intolerance
  - Other

- Release of cytokines
  - IL-6
  - TNF-α
  - Adiponectin
  - Other adipokines

- Lack of or dysfunctional subcutaneous fat
  - Impaired clearance and storage of TG in subcutaneous fat

- Hypertriglyceridemia

Altered metabolic profile:
- Insulin-resistant milieu
- Proinflammatory state
- Prothrombotic state
- Prohypertensive state

- Ectopic fat deposition
ongoing debate, insulin resistance has been shown to be strongly associated with components of the atherogenic, prothrombotic, and inflammatory profile seen in individuals with cardiometabolic risk factors.

Adipose insulin resistance has been implicated as a key component of cardiometabolic risk, with heightened release of FFAs secondary to increased lipolysis. In the liver, increased FFA flux results in the increased production of glucose and TGs and secretion of very low-density lipoprotein. Associated lipid and lipoprotein abnormalities include reductions in HDL-C and increased density of low-density lipoprotein (LDL). FFAs also reduce insulin sensitivity in muscle and contribute to increased pancreatic insulin secretion, resulting in hyperinsulinemia. Hyperinsulinemia (and possibly increased FFA levels) may result in enhanced sodium reabsorption and hyperinsulinemia. Hyperinsulinemia (and possibly increased FFA levels) may result in enhanced sodium reabsorption and increased sympathetic nervous system activity and may contribute to the development of hypertension.

In addition, there are paracrine and endocrine effects of the proinflammatory state. A variety of cells in adipose tissue (eg, adipocytes and monocyte-derived macrophages) enhance secretion of interleukin-6 and tumour necrosis factor-α, resulting in more insulin resistance and lipolysis of adipose tissue TG stores, resulting in further increased circulating FFAs. Cytokines and FFAs increase the production of fibrinogen, CRP, and plasminogen activator inhibitor-1 (PAI-1) by the liver, complementing the overproduction of plasminogen activator inhibitor-1 by adipose tissue. This process results in a prothrombotic state.

What are the contributions of adipokines to insulin resistance and endothelial dysfunction?

Mature adipocytes are active endocrine and paracrine organs secreting numerous mediators that participate in diverse metabolic processes. Fat-derived molecules (eg, lipoprotein lipase and cholesterol ester transfer protein) act via endocrine, paracrine, autocrine, and/or juxtacrine modes of action to modulate fat depot size and body fat redistribution and ultimately influence the levels of secretory proteins. More recently, adipose tissue has been recognized as a rich source of proinflammatory mediators (adipokines) that may directly contribute to vascular injury, insulin resistance, and atherogenesis. It is also the source of adiponectin, a potent insulin-sensitizing, anti-inflammatory, and antiatherosclerotic protein, the levels of which are reduced in states of insulin resistance, obesity, and diabetes.

Both FFAs and hyperglycemia contribute to mechanisms known to promote atherosclerosis. Even short excursions of these 2 metabolites have profound consequences, and combined excursions mainly observed in the postprandial state are believed to be synergistic for the toxic effect.

Summary

The clustering of risk factors that constitute cardiometabolic risk—dyslipidemia, elevated BP, dysglycemia, prothrombotic state, and inflammatory state—might be the consequence of a complex interplay between various tissues (mainly adipose tissue and liver). The phenotype of the person with high cardiometabolic risk is characterized by overweight or obesity with preferential android fat accumulation, sedentary lifestyle, and diet high in total or saturated fats. Interestingly, some obese patients remain insulin sensitive despite enlarged fat mass but low visceral adipose tissue accumulation, while some normal-weight subjects display significant insulin resistance despite apparently normal weight but excessive abdominal obesity. This suggests that factors in addition to excessive fat mass affect adipose tissue functionality.

Identification of Cardiometabolic Risk

P.A. McFarlane, R. Lewanczuk, R. McPherson, and P. Poirier

Cardiometabolic risk refers to the sum of risk factors that increase an individual’s risk of having a CV event or developing metabolic abnormalities such as type 2 diabetes (see Fig. 1). This risk is generated by traditional CV risk factors such as hypertension or smoking, by nontraditional risk factors such as insulin resistance, and by other genetic and clinical factors that are not fully understood. There is interplay between the various risk factors (eg, hyperglycemia can exacerbate hypertriglyceridemia), and there is overlap between the main outcomes (eg, people who develop type 2 diabetes are at higher risk for CV events). 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.

Who should undergo cardiometabolic risk assessment?

An assessment should occur when any traditional CV risk factor, such as hypertension or dyslipidemia, is first identified or in patients who are overweight or obese, especially those who are abnormally obese. Figure 4 describes the general approach to assessing cardiometabolic risk.

How should cardiometabolic risk be assessed?

Height, weight, body mass index and waist circumference.

Height, weight, body mass index (BMI; see Table 3), and waist circumference should be measured (with the use of the ethnic-specific cutoffs in Table 1) as part of an assessment of cardiometabolic risk. Ideally, height is measured by a stadiometer. Weight should be measured by an accurately calibrated scale. Various methods for measuring waist circumference have been proposed. A recent expert consensus panel recognized that the method described in Table 4 for measuring waist circumference might be more readily adopted by physicians (and by the general public for self-measurement) as it requires a single palpation to locate the iliac crest. The “spin” or “orbit” techniques are alternate methods that can be considered to facilitate encouraging the abdomen with the measuring tape (see Table 5) and provide the patient with choice. However, the differences between commonly used waist circumference measurement protocols have no substantial influence on the association between waist circumference and morbidity of CVD and diabetes and all-cause mortality and CVD mortality. Patient preference and level of comfort with being measured should therefore be considered when choosing a measurement technique.

BP. Hypertension is an important element of cardiometabolic risk. Patients should have their BP accurately assessed at the time of screening for cardiometabolic risk. Ideally, BP should be measured using the technique described in Table 6.
It is important to note that half of overweight individuals with high normal BP will develop hypertension within the next 2 years.91 These individuals should be monitored periodically for the development of hypertension.

Renal disease. In Canada, the most common cause of chronic kidney disease is diabetes, followed by ischemic nephropathy from causes such as renovascular disease and hypertensive nephrosclerosis.92 As many as half of people with diabetes will develop chronic kidney disease, and the risk for end-stage renal disease is between 2.5 and 4.25 times higher in people with hypertension than in normotensive individuals.93,94 The population of people with elevated cardiometabolic risk will have a high prevalence of conditions such as diabetes, hypertension, or general vascular disease, all of which are conditions that place an individual at high risk for chronic kidney disease. For this reason, people with elevated cardiometabolic risk should be screened for signs of kidney disease, including persistent proteinuria or an inappropriately low glomerular filtration rate (as estimated using the serum creatinine). As blockers of the renin-angiotensin-aldosterone system (RAAS) such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are frequently indicated in this population, and these medications can raise serum creatinine and potassium levels,95,96 measuring serum electrolytes and creatinine in this population is indicated in order to determine a baseline for medication safety monitoring. Finally, patients with generalized vascular disease are at higher risk for the development of secondary hypertension in the form of renal vascular disease. Suspicion for a hyperaldosterone state is increased in those with unexplained hypokalemia.97

Laboratory tests. If the patient has a known traditional CV risk factor or is overweight or obese or has a large waist circumference, then an FPG and fasting lipid profile (total cholesterol, HDL-C, LDL cholesterol [LDL-C], and TGs) should be obtained. Apo B can be used in place of LDL-C (see the section titled Pharmacologic and Surgical Interventions to Reduce Cardiometabolic Risk). These tests should be obtained in individuals who reach either the Canadian Diabetes Association98 or the Canadian Cardiovascular Society (CCS)99 screening thresholds according to the criteria summarized in Table 7. The BP, glycemia, and lipid diagnostic thresholds and thresholds for initiation of treatment are listed in Table 8. For the purpose of interpreting the lipid tests, the FRS can be used. Those with a 10-year CV risk ≥20% or with diabetes are considered at high risk for CV events, those with a 10-year CV risk of 10% to 19% are at moderate risk, and those with a 10-year CV risk <10% are considered at low risk. Treatment targets are summarized in Table 9.

Table 3. Body weight classification by BMI in adults

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>Normal</td>
</tr>
<tr>
<td>25.0-29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30.0-34.9</td>
<td>Obese (class I)</td>
</tr>
<tr>
<td>35.0-39.9</td>
<td>Obese (class II)</td>
</tr>
<tr>
<td>≥40.0</td>
<td>Obese (class III)</td>
</tr>
</tbody>
</table>

In a recent advisory statement, the American Heart Association97 recommended further subdividing obesity (BMI ≥ 30.0 kg/m²) into 5 categories by adding class IV (≥50.0 kg/m²) and class V (≥60.0 kg/m²) obesity. BMI, body mass index (weight in kilograms / height in metres²).

* BMI values are age and gender independent and may not be correct for all ethnic populations.

Table 4. Recommended technique to measure waist circumference

1. Locate the upper hipbone and the top of the right iliac crest.
2. Position the measuring tape in a horizontal plane around the abdomen at the top of the iliac crest.
3. Fit the measuring tape snugly (but not compressing the skin) around the person, with the tape horizontal to the ground.
4. Measure at the end of a normal expiration with the person’s abdominal muscles relaxed.
Table 5. Alternate techniques to measure waist circumference

Spin technique
1. Ask the patient to hold one end of the measuring tape against the midline of his or her abdomen.
2. The patient carefully spins 360 degrees while the clinician holds the other end of the measuring tape.
3. Once the patient has completed the spin, the tape should be wrapped around his or her abdomen.
4. Adjust the position of the tape, so it fits snugly (but not compressing the skin) around the patient, with the tape horizontal to the ground.
5. Measure at the end of a normal expiration with the patient’s abdominal muscles relaxed.

Orbit technique
1. For patients in whom performing the spin is unsafe or not possible, the “orbit” technique can be used.
2. Ask the patient to hold one end of the measuring tape against the midline of his or her abdomen.
3. While holding the other end of the tape, the clinician then walks around the patient, wrapping the tape around the abdomen in the process.
4. Adjust the position of the tape, so it fits snugly (but not compressing the skin) around the patient, with the tape horizontal to the ground.
5. Measure at the end of a normal expiration with the patient’s abdominal muscles relaxed.

Table 6. Recommended technique for measuring blood pressure

1. The patient should be seated comfortably in a chair with both feet on the floor.
2. A calibrated sphygmomanometer or automated monitor should be used:
   a) If an automated monitor is used, the monitor should be placed at approximately the same height as the heart, and the arm that is being assessed should be comfortably supported at the same height.
   b) If a sphygmomanometer is used, the valve should be opened such that the mercury does not fall more than 5 mm Hg per second, and the systolic and diastolic values should not be rounded off.
3. If the arm circumference is <31 cm (<12.2 inches), a regular-sized cuff can be used; otherwise, a large cuff should be used.
4. No talking or other distractions should occur during the reading.
5. Ideally, at least 3 readings should be performed. The first reading should be discarded, and the average of the subsequent readings should be taken.
6. Blood pressure should be taken in both arms. The arm showing the higher readings is likely to be the most accurate, and subsequent readings should be performed in that arm.
7. Unattended blood pressure readings (ie, those done by an automated device while the patient is alone in the examination room) may be more accurate.
8. Acceptable alternatives are 24-hour ambulatory blood pressure monitoring or proper self-measurements.

Table 7. Thresholds and criteria for screening for dyslipidemia and dysglycemia

<table>
<thead>
<tr>
<th>Factor</th>
<th>Screen with fasting lipid profile and FPG if any of the following factors are present.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>FPG in those aged ≥40 years, or earlier in those with risk factors listed below</td>
</tr>
<tr>
<td></td>
<td>Fasting lipid profile in men aged ≥40 years</td>
</tr>
<tr>
<td></td>
<td>and women aged ≥50 years (or postmenopausal), or earlier in those with risk factors listed below</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Known to be hypertensive</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Known to have dyslipidemia</td>
</tr>
<tr>
<td>Glyceria</td>
<td>Known to have diabetes, IFG, or IGT</td>
</tr>
<tr>
<td>Family history</td>
<td>Early CAD (first-degree relative aged &lt;60 years)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Aborginal</td>
</tr>
<tr>
<td></td>
<td>South Asian</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
</tr>
<tr>
<td>Smoking</td>
<td>Current or former (within 1 year) smoker</td>
</tr>
<tr>
<td>Other medical conditions</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td></td>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td></td>
<td>Polycystic ovary syndrome</td>
</tr>
<tr>
<td></td>
<td>Acanthosis nigricans</td>
</tr>
<tr>
<td></td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>Size</td>
<td>Overweight and/or abdominal obesity</td>
</tr>
<tr>
<td>Complications</td>
<td>Manifestations of dyslipidemia or complications of diabetes</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>History of delivery of macrosomic infant and/or gestational diabetes mellitus</td>
</tr>
<tr>
<td>Vascular history</td>
<td>Vascular disease (coronary, cerebral, vascular)</td>
</tr>
<tr>
<td></td>
<td>or symptoms (exertional chest discomfort, dyspnea, erectile dysfunction)</td>
</tr>
</tbody>
</table>

Summary

Screening for traditional and nontraditional risk factors provides a comprehensive picture of a patient’s risk for cardiometabolic events. Screening should occur when any traditional risk factor is first identified or if a patient is overweight or obese, and it should include physical examination, history, and laboratory and other tests as indicated by patient age, existing risk factors, or guideline-recommended criteria.

Health Behaviour Interventions to Reduce Cardiometabolic Risk


Cardiometabolic risk represents global CVD risk related to well-established risk factors (age, sex, family history, smoking, BP, LDL-C, HDL-C, diabetes) and emerging factors such as dysglycemia and familial dyslipidemia.
Abdominal obesity and related metabolic abnormalities often referred to as metabolic syndrome. On that basis, traditional CVD risk factors should be managed by following current guidelines.11,12,90,98-101

Health behaviour modification is recommended as the primary treatment strategy for management of cardiometabolic risk.11,12,90,98-101 Attempts to modify health behaviour should include simultaneous counselling regarding physical activity, caloric intake, and diet composition, as well as smoking cessation (see page e19).

Abdominal obesity

What is the effect of exercise on abdominal obesity? Chronic exercise is generally associated with reduction in abdominal obesity as measured by waist circumference, and the degree of waist circumference reduction achieved is linearly related to the magnitude of weight loss.102 Not surprisingly, a considerable interindividual variation (±40%) in the magnitude of change in waist circumference is reported.103 In general, those studies that prescribe the greatest amount of moderate physical activity (~60 minutes per day), and thus induce the greatest negative energy balance and weight reduction (~8.0 kg), generally report the largest reductions in waist circumference (~7.0 cm), independent of gender.103,104 More modest exercise prescriptions (~30 minutes per day) often lead to smaller reductions in waist circumference (1.0-3.0 cm).103,106

Regular exercise is also consistently associated with reductions in visceral fat.102,107 As expected, the greatest exercise

### Table 8. Tests and diagnostic criteria and thresholds for treatment

<table>
<thead>
<tr>
<th>Test</th>
<th>Diagnostic criteria or thresholds for treatment</th>
</tr>
</thead>
</table>
| **Blood glucose**98 | Fasting <6.1 and 2h 7.8-11.0 mmol/L = isolated IGT  
Fasting 6.1-6.9 mmol/L and 2h <7.8 mmol/L = isolated IFG  
Fasting 6.1-6.9 mmol/L and 2h 7.8-11.0 mmol/L = IFG and IGT  
Fasting ≥7.0 mmol/L or 2h ≥11.1 mmol/L = diabetes |

| **Blood pressure**98,99 | Diabetes or CKD ≥130 mm Hg SBP or ≥80 mm Hg DBP  
No diabetes or chronic kidney disease:  
- Office readings: ≥160 mm Hg SBP or ≥100 mm Hg DBP averaged over 3 visits or ≥140 mm Hg SBP or ≥90 mm Hg averaged over 5 visits  
- Home readings ≥135 mm Hg SBP or ≥85 mm Hg DBP  
- 24-hour BP monitor daytime average ≥135 mm Hg SBP or ≥85 mm Hg DBP  
- 24-hour BP monitor average ≥130 mm Hg SBP or ≥80 mm Hg DBP  
- Unattended automated office BP ≥135 mm Hg SBP or ≥85 mm Hg DBP  
High risk for CVD: Consider treatment in all patients  
Moderate risk for CVD:  
- LDL-C > 3.5 mmol/L TC/  
- hs-CRP > 2 mg/L (in men aged >50 years or women aged >60 years)  
- Family history and hs-CRP modulates risk  
Low risk for CVD: Treat if:  
- LDL-C ≥ 5.0 mmol/L |

BP, blood pressure; CHEP, Canadian Hypertension Education Program; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; HT, hypertension; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; LDL-C, low-density lipoprotein cholesterol; OGTT, oral glucose tolerance test; SBP, systolic blood pressure; TC, total cholesterol.

### Table 9. Treatment targets

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Target</th>
</tr>
</thead>
</table>
| **Blood glucose**98 | A1C* ≤ 7.0%  
CKD or diabetes: <130/80 mm Hg  
Otherwise: <140/90 mm Hg |
| **BP**98 |  
Apo B < 0.80 g/L |
| **Lipids**99 | Risk level  
Primary target  
Alternate primary target |
| High | LDL-C < 2.0 mmol/L  
(or ≥50% reduction in LDL-C)  
Apo B < 0.80 g/L |
| Moderate | LDL-C < 2.0 mmol/L  
(or ≥50% reduction in LDL-C)  
Apo B < 0.80 g/L |
| Low | ≥50% reduction in LDL-C  
NA |

A1C, glycated hemoglobin; apo B, apolipoprotein B; BP, blood pressure; CKD, chronic kidney disease; LDL-C, low-density lipoprotein cholesterol; NA, not applicable.

*When setting treatment goals and strategies, consideration should be given to individuals’ risk factors such as age, prognosis, presence of risk factors, and comorbidities.
What is the effect of caloric restriction on abdominal obesity? Caloric restriction is consistently reported to decrease waist circumference in obese men and women. For example, reducing caloric intake by 700 kcal per day for 3 months resulted in a 7.0-cm reduction in waist circumference concurrent with a 7.5-kg weight loss in obese men. Similar results were also reported in a sample of obese, premenopausal women. Combined evidence from several studies suggests that each kilogram of weight lost because of caloric restriction alone is associated with an approximately 1.0-cm decrease in waist circumference.

With regard to visceral fat, the strictest diets (very low caloric diets [VLCDs] with energy intake of 800-1200 kcal per day) of 3 to 6 months’ duration, tend to result in the greatest reductions in weight (10-18 kg) and visceral fat (24%-47%). However, it should be noted that in 1998, a US National Heart, Lung, and Blood Institute expert panel recommended against the use of VLCDs based on studies that demonstrated no difference in long-term weight reduction between VLCDs and low-calorie diets, as there was greater weight regain with VLCDs.

Glucose metabolism

What is the effect of exercise on glucose metabolism? Significant reductions in FPG levels are consistently observed in people with type 2 diabetes in response to a single exercise bout. This effect, however, is exclusive to those with significantly elevated plasma glucose values as an acute exercise bout in individuals without diabetes (with relatively normal blood glucose levels) has no appreciable effect on plasma glucose values.

Significant improvements in insulin resistance, as measured by the rate of glucose clearance during a euglycemic-hyperinsulineic clamp, have been achieved after approximately 1 hour of moderate-intensity exercise in obese people with type 2 diabetes and in normoglycemic individuals, insulin-resistant individuals, people with type 2 diabetes, and healthy individuals. (In contrast, most clinical trials have not demonstrated a beneficial effect of glycemic control in people with type 1 diabetes. The effects of physical activity on glycemic control in this population are beyond the scope of this document.) The magnitude of improvement in insulin sensitivity after a single exercise bout ranges from 15% to 24%—improvements that are equivalent in magnitude to those achieved through chronic pharmacologic intervention.

What is the effect of caloric restriction on dyslipidemia? A meta-analysis of 10 intervention studies in people with type 2 diabetes concluded that VLCDs (800 kcal per day) of at least 3 months’ duration resulted in a 25% to 30% reduction in FPG levels, with the degree of plasma glucose reduction linearly related to the amount of weight lost. However, as with exercise, caloric restriction does not appear to affect FPG levels in subjects with normal baseline values.

Caloric restriction of 3 to 4 months’ duration is associated with improvements in insulin resistance of 17% to 72%, with VLCDs associated with improvements in the upper range (eg, 72%), and more modest caloric restriction (700-kcal reduction per day) associated with improvements of approximately 43% in 1 study. VLCDs, however, are generally not recommended for obesity-management programs.

Three large randomized controlled trials (RCTs), the US Diabetes Prevention Program, the Finnish Diabetes Prevention Study, and the Chinese Da Qing Study, provide compelling evidence that intensive health behaviour intervention can prevent or delay the development of diabetes in individuals with impaired glucose tolerance (IGT). In the Diabetes Prevention Program and Diabetes Prevention Study, the independent effects of physical activity vs dietary modification were unclear; thus in Table 10, we describe the overall effects of health behaviour change. Comprehensive intervention programs based on health behaviours can reduce risk of progression to diabetes to a greater degree than can be achieved with some pharmacologic interventions.

Intensive health behaviour intervention has also been shown to be highly effective in improving diabetes control and CV risk factors in overweight or obese people with type 2 diabetes. The ongoing, multicentre, Look AHEAD (Action for Health in Diabetes) trial, sponsored by the US National Institutes of Health, is designed to determine whether CV morbidity and mortality in individuals with type 2 diabetes can be reduced through intensive health behaviour modification. The 1-year results from the trial demonstrated that a mean weight loss of 8.6% resulted in significant improvement in glycemic control (0.7% absolute lowering in A1C), TGs, and HDL-C levels, as well as decreased systolic and diastolic BP values and reductions in diabetes, hypertension, and lipid-lowering medications.

Dyslipidemia

The atherogenic lipid profile consists of hypertriglyceridemia, low levels of HDL-C, and high levels of LDL-C, in particular small and dense LDL particles.

What is the effect of exercise on dyslipidemia? The evidence for beneficial lipid changes due to chronic physical activity is strongest for HDL-C and TGs. Results of several
interventions reveal that overall, 30 to 60 minutes of aerobic physical activity, 3 to 5 times per week, at a moderate intensity results in a mean increase in HDL-C levels of ~4% (0.05 mmol/L), predominantly as a result of increases in the HDL2-C subfraction,140,142,143 and a decrease in TG levels of ~12% (0.21 mmol/L).140 Others have concluded that physical activity that induces an energy expenditure of 1200 to 2200 kcal per week may bring about a 4% to 22% (0.05-0.21 mmol/L) increase in HDL-C levels and a 4% to 37% (0.01-0.43 mmol/L) decrease in TG levels.138 A recent meta-analysis suggested that a minimal weekly aerobic exercise volume of ~900 kcal or 120 minutes per week is required to increase HDL-C levels by 0.065 mmol/L.144

In contrast to the consistent findings for HDL-C and TGs, the available evidence suggests that chronic physical activity does not significantly alter the levels of LDL-C.138,140 Daily aerobic activity of at least 25 minutes’ duration can, however, increase the mean LDL particle size.135 It appears that LDL particle size is as important as total LDL-C levels in predicting cardiometabolic risk. For example, analyses from the Quebec Cardiovascular Study demonstrated that a higher proportion of small LDL particles predicted incidence of ischemic heart disease, independent of total LDL-C levels.145

While some suggest that exercise-induced weight loss must be achieved in order to observe improvements in lipid profile,137 others have shown that improvements in HDL-C and TGs are observed even when weight remains unchanged.138,140,146 Changes may be mediated by improvements in body composition, such as increases in skeletal muscle mass or reductions in visceral fat.104,105

What is the effect of caloric restriction on dyslipidemia? A meta-analysis based on evidence from 64 individual studies revealed that TG levels are reduced by ~32% (0.66 mmol/L) in response to various calorie-restriction protocols that resulted in an average 16.6-kg weight loss.147 Caloric restriction is also associated with modest increases in HDL-C levels, although the relationship is not as straightforward as that observed for TG levels. Specifically, caloric restriction results in a transient decrease in HDL-C levels,147,148 but once body weight has stabilized and a new energy balance has been achieved, HDL-C levels increase above baseline.147 Active weight loss reduces HDL-C by an average of 8%, followed by a 12% increase above baseline once weight had stabilized.147 The effects of caloric restriction on LDL-C are well established, with an 11% reduction reported after mean weight loss of 16.6 kg.147

Elevated BP

What is the effect of exercise on elevated BP? It is well documented that regular aerobic physical activity reduces systolic and diastolic BP149-155 in lean,149,154 obese,149,154 hypertensive,149,152,153 and normotensive149,150,152 individuals. The results of various reviews and meta-analyses suggest that independent of age and BMI, 40 minutes of moderate-intensity physical activity performed 3 times per week reduces systolic BP by 3 to 11 mm Hg and diastolic BP by 3 to 8 mm Hg.149-155 Further, the BP reductions are significantly greater among hypertensive vs normotensive individuals (7 and 5 mm Hg vs 2 and 2 mm Hg reductions in systolic BP and diastolic BP, respectively).155 Exercise-induced BP reductions do not appear to be related to alterations in body weight or abdominal obesity.155

What is the effect of caloric restriction on elevated BP? Caloric restriction modestly decreases BP in men and women. A meta-analysis of 25 RCTs involving 4874 subjects showed

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**Table 10. Summary of health behaviour intervention trials to prevent progression from impaired glucose tolerance to type 2 diabetes**

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Intervention</th>
<th>Mean follow-up (years)</th>
<th>Risk reduction for type 2 diabetes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Da Qing130</td>
<td>577</td>
<td>Diet</td>
<td>6</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exercise</td>
<td></td>
<td>46</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diet + exercise</td>
<td>2.8</td>
<td>58</td>
</tr>
<tr>
<td>DPS127</td>
<td>3234</td>
<td>Intensive health behaviour modification (dietary modification, weight reduction goal of 7% of initial body weight, and 150 minutes per week of moderate-intensity physical activity)</td>
<td>3.2</td>
<td>58</td>
</tr>
<tr>
<td>DPS126</td>
<td>522</td>
<td>Intensive health behaviour modification (goals were 7% weight loss, &lt;30% of total energy from fat, &lt;10% of total energy from saturated fat, ≥15 g fibre/1000 kcal/day; moderate-intensity exercise for ≥30 minutes per day)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DPP, Diabetes Prevention Program; DPS, Diabetes Prevention Study.

---

**Table 11. Summary of pharmacologic intervention trials to prevent progression from impaired glucose tolerance to type 2 diabetes**

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Intervention</th>
<th>Follow-up (years)</th>
<th>Risk reduction for type 2 diabetes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPP126</td>
<td>3234</td>
<td>Metformin (Glucophage)</td>
<td>3.2 (mean)</td>
<td>31</td>
</tr>
<tr>
<td>STOP-NIDDM131</td>
<td>1429</td>
<td>Acarbose (Glucobay)</td>
<td>3.9 (median)</td>
<td>32</td>
</tr>
<tr>
<td>XENDOS135</td>
<td>3305</td>
<td>Xenical (orlistat)</td>
<td>4</td>
<td>45</td>
</tr>
<tr>
<td>DREAM132</td>
<td>5269</td>
<td>Rosiglitazone (Avandia)</td>
<td>3 (median)</td>
<td>60</td>
</tr>
<tr>
<td>CANOE133</td>
<td>207</td>
<td>Rosiglitazone + metformin (Avandamet)</td>
<td>3.9 (median)</td>
<td>66</td>
</tr>
</tbody>
</table>

CANOE, Canadian Normoglycemia Outcomes Evaluation; DPP, Diabetes Prevention Program; DREAM, Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication; STOP-NIDDM, Study to Prevent Non Insulin Dependent Diabetes; XENDOS, Xenical in the Prevention of Diabetes in Obese Subjects.
that caloric restriction that induced a mean weight loss of 6.7 kg was associated with a 5- and 4-mm Hg reduction in systolic and diastolic BP, respectively.156 A later meta-analysis of 11 trials reported similar diet-induced BP reductions.157 Exercise- and diet-induced reductions in BP are thus modest and rarely of sufficient magnitude to achieve normotension.158 Significant decrements in health risk are expected, however, even with marginal reductions in BP.159

What is the impact of dietary composition on cardiometabolic risk?

Although a detailed consideration of the effects of diet composition on the components of cardiometabolic risk is beyond the scope of this review, a number of excellent reviews are available. Dietary modification is recommended by Health Canada163 and others98,166 as one of the key health behaviour–based strategies to reduce CV risk (see Table 12).98,164,165 Furthermore, the 2006 Canadian Clinical Practice Guidelines on the Management and Prevention of Obesity101 present dietary intervention recommendations appropriate for weight loss and management. Regardless of the macronutrient composition, the most important nutritional consideration in improving cardiometabolic risk appears to be caloric reduction.101 Sugar-sweetened beverages are the greatest contributor to added-sugar intake in the United States and may promote weight gain because caloric intake at subsequent meals is not reduced to compensate for these liquid calories. As these beverages provide little nutritional value and may also increase the risk of type 2 diabetes and CVD independently of obesity, intake should be limited and should be replaced by healthy alternatives such as water.166 Limiting dietary sodium intake to a maximum of 1500 mg per day for those aged ≥50 years, 1300 mg per day for those aged 51 to 70 years, and 1200 mg per day for those aged ≥71 years is recommended for all adult Canadians to prevent and control hypertension.90

Brief interactive dietary assessment tools are available from Health Canada (http://www.canadasfoodguide.org)163 and Dietitians of Canada (http://www.eatracker.ca).167,168 These tools provide information suitable for the general public regarding how their eating habits compare with Health Canada recommendations. In addition, tools and resources for health care professionals and the general public regarding dietary sodium are available from the Canadian Hypertension Education Program (CHEP; http://hypertension.ca/chep).90

How can physicians help their patients adopt and maintain healthy lifestyle behaviours?

Family physicians have described many barriers to incorporating health behaviour counselling into primary care. These include lack of time, lack of counselling expertise, limited clinical resources, lack of support from the health care system, and the perception that patients are uninterested in changing health behaviour habits.168

Until recently, the effectiveness of health behaviour counselling interventions delivered by primary care providers on health outcomes was unclear. Fleming and Godwin169 concluded that primary care–based counselling of adults at low CV risk had modest benefit on metabolic risk factors including BP, lipids, CV risk scores, and body weight, even in tightly controlled RCTs. Other literature reviews have reached similar conclusions.169,170

Recent evidence, however, suggests that health behaviour–based counselling by primary care providers (nurses and kinesiologists) can promote long-term increased physical activity among formerly sedentary women171 and long-term weight maintenance among overweight women.172 Although reasons for success were not examined in those trials, other studies have consistently identified factors that can reinforce messages and sustain health behaviour changes, including frequent or ongoing telephone support, follow-up of missed appointments, work with peer or family members to support health behaviour changes, and self-monitoring of body weight.173,174 Also, it appears that walking is as effective as expensive centre-based exercise classes, especially for older adults.173

Nutrition therapy, including counselling by registered dietitians, has been demonstrated to effectively decrease body weight and several metabolic measures (eg, blood lipids, A1C, BP) in individuals who are overweight or have diabetes, dyslipidaemia, and/or hypertension.175

There is a growing consensus that counselling in primary care requires a multidisciplinary approach.98,101 It is clear that although family physicians have a very important role in identifying people with increased cardiometabolic risk, they 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.

Summary

The weighted evidence shows that modifications in health behaviours (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 per day]) will result in significant reductions in cardiometabolic risk (see Table 13).
Regular exercise is associated with improvements in abdominal obesity, visceral fat, FPG, insulin resistance, TGs, HDL-C, and systolic and diastolic BP. Caloric restriction is associated with improvements in abdominal obesity, visceral fat, FPG, insulin resistance, LDL-C, TGs, and HDL-C, and with modest improvements in BP. Comprehensive and sustained modifications in health behaviours can also significantly reduce the risk for type 2 diabetes and improve metabolic control and CVD risk factors in people with type 2 diabetes. The magnitude of improvement in these variables appears to be dependent on baseline values, with greater improvements reported among those with the greatest disturbances in metabolic status. 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 in the absence of significant weight change.

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. Despite the expected benefits and significant reductions in morbidity associated with health behaviour change, the positive impact of health behaviour interventions on mortality has yet to be demonstrated. Further, the effect of health behaviour interventions on CV events is not yet known. The Look AHEAD trial may provide much-needed insight into the potential association. Short-term effects of health behaviour modification on glucose and metabolic risk factors are promising, but long-term data are required in order to elucidate the effects on the microvascular complications of diabetes and CVD.

**Pharmacologic and Surgical Interventions to Reduce Cardiometabolic Risk**


The adoption of healthy behaviour is the most fundamental therapeutic strategy for the individual at increased cardiometabolic risk. Clinical trial evidence shows that weight loss and increased physical activity are very effective in reversing cardiometabolic risk. However, these health behaviour modifications are often difficult to achieve and sustain long-term. Thus, pharmacologic therapy or surgery may be required as an adjunct to health behaviour intervention to optimally reduce cardiometabolic risk.

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. Yet there are very few clinical trials that evaluate treatment for individuals with cardiometabolic risk without either concomitant diabetes or established CVD.

**Who should receive weight loss medications?**

In addition to health behaviour modification, pharmacologic approaches may be required to manage obesity. Since obesity, especially abdominal obesity, is a key component of cardiometabolic risk, reductions in body weight and waist circumference are important first steps in any management strategy, to be achieved primarily through diet and increased physical activity. Of note, visceral fat depot will be the first fat depot to be mobilized through these approaches.

Weight-loss medications should be used only in association with a weight-reducing diet and increased physical activity. For patients with a BMI $\geq 30$ kg/m², or those with a BMI $\geq 27$ kg/m² plus CV risk factors and/or 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. (See Table 3.) 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.

In Canada, 2 prescription drugs are approved for weight loss, the gastrointestinal lipase inhibitor orlistat and the serotonin and norepinephrine reuptake inhibitor sibutramine. Clinical trials using either agent have demonstrated weight loss of approximately 6 to 7 kg during 1 to 2 years, compared with 2 to 3 kg with diet alone. Studies of clinical outcomes for both agents are as yet limited. However, weight-loss medications appear to have beneficial effects on the CV system. The Xenical in the Prevention of Diabetes in Obese Subjects trial showed that orlistat treatment for 4 years decreased the risk of

### Table 13. Effects of health behaviour modification on cardiometabolic risk

<table>
<thead>
<tr>
<th>Cardiometabolic risk factor</th>
<th>Effect of chronic exercise*</th>
<th>Effect of chronic caloric restriction**</th>
</tr>
</thead>
<tbody>
<tr>
<td>WC</td>
<td>$-3.0$ to $-0.7$ cm ($-6%$)</td>
<td>$-4$ to $-7$ cm ($-6%$)</td>
</tr>
<tr>
<td>TGs</td>
<td>$-0.21$ mmol/L ($-12%$)</td>
<td>$-0.12$ mmol/L ($-6%$)</td>
</tr>
<tr>
<td>HDL-C</td>
<td>$+0.05$ mmol/L ($+4%$)</td>
<td>$+0.07$ mmol/L ($+6%$)</td>
</tr>
<tr>
<td>LDL-C</td>
<td>Increased LDL particle size</td>
<td>$-0.39$ mmol/L ($-11%$)</td>
</tr>
<tr>
<td>FPG</td>
<td>Negligible</td>
<td>Negligible</td>
</tr>
<tr>
<td>Person without diabetes</td>
<td>$-1.5$ mmol/L ($-15%$)</td>
<td>$-1.2$ mmol/L ($-15%$)</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>$+32%$ to $+85%$</td>
<td>$+17%$ to $+72%$</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>Combination of physical activity and diet: 31% to 58% relative risk reduction</td>
<td></td>
</tr>
<tr>
<td>BP</td>
<td>$-4$ mm Hg</td>
<td>$-5$ mm Hg</td>
</tr>
<tr>
<td>Systolic</td>
<td>$-3$ mm Hg</td>
<td>$-4$ mm Hg</td>
</tr>
<tr>
<td>Diastolic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Moderate-intensity exercise = 3-5 d/wk; 30-60 min/d.
** 500-700-kcal daily caloric restriction.
developing type 2 diabetes in patients with IGT, yet in individuals with normal baseline glucose tolerance, new IGT and diabetes were not prevented. A meta-analysis indicates that sibutramine-induced weight loss is also associated with improved glycemic control. The Sibutramine Cardiovascular Outcomes trial assessed the impact of sibutramine on morbidity and mortality in obese patients with established CV disease, diabetes, or both 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 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.

There is insufficient evidence to recommend in favour of or against the use of herbal remedies, dietary supplements, or homoeopathy for weight management in the obese person.

**Who should be considered for bariatric surgery?**

Bariatric surgery has been shown to lower all-cause mortality by 24% to 40% because of a reduction in deaths from myocardial infarction (MI), diabetes, and cancer and to prevent the development of diabetes in patients with severe obesity. Currently, bariatric surgery can be considered in individuals with class III or above obesity (ie, BMI ≥ 40 kg/m²) or those with class II obesity (ie, BMI ≥ 35 kg/m²) plus comorbid conditions.

Bariatric surgery has a low operative mortality (<1%) if performed by an experienced team. Surgical intervention results in sustained weight loss, improvement in comorbidities, and increased survival. However, late complications may arise from both nutritional deficiencies and behavioural changes. The best outcomes are achieved in high-volume, comprehensive bariatric centres, with an interdisciplinary team dedicated to long-term follow-up. Bariatric surgery is indicated for patients who have severe obesity, in whom efforts at medical therapy have failed, and who have an acceptable operative risk. Following bariatric surgery, patients report improvements in their quality of life, social interactions, psychological well-being, employment opportunities, and economic condition.

**Lipid control**

Statin therapy reduces adverse CV risk in persons with diabetes, irrespective of the baseline LDL-C. The Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) showed that lovastatin 20 to 40 mg reduced major CV events by 37% in subjects with no history of vascular disease and average LDL-C levels, yet lower than average HDL-C (35% had HDL-C < 0.91 mmol/L). The population mean BMI was 26 to 27 kg/m², and the median hs-CRP was 1.6 mg/L. Hence, it is likely that a significant proportion of the population had cardiometabolic risk factors. A post hoc analysis indicated that in individuals with LDL-C below the median LDL-C, the benefit of statin treatment was limited to those with an elevated hs-CRP level. The randomized trial of rosuvastatin in the primary prevention of cardiovascular events among individuals with low levels of LDL-C and elevated levels of CRP (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin [JUPITER]) showed that women aged >60 years and men aged >50 years with LDL-C < 3.4 mmol/L and hs-CRP > 2 mg/L benefited from rosuvastatin 20 mg daily (44% reduction in the primary endpoint [MI, stroke, arterial revascularization, hospitalization for unstable angina, or death from CV causes] and 37% reduction in the combined endpoint of nonfatal MI, nonfatal stroke, or death from CV causes). Subgroup analysis showed similar relative hazard ratio reductions in the rosuvastatin group in every subgroup analysis, including those with or without metabolic syndrome and those with or without a BMI > 25 kg/m² or BMI >30 kg/m². Over 40% of individuals were noted to meet the most recent criteria of the National Cholesterol Education Program Adult Treatment Panel III for metabolic syndrome, and the median BMI was 28.1 kg/m². The Anglo-Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm, in patients with hypertension and 3 additional CV risk factors, demonstrated that atorvastatin 10 mg daily reduced CV events by 36% during approximately 3 years. Many individuals with cardiometabolic risk have hypertension with additional CV risk factors and will consequently benefit from statin therapy. (See Tables 8 and 9.)

**Which patients with cardiometabolic risk should receive statin therapy?**

Current CCS dyslipidemia guidelines indicate that the decision to institute statin therapy should be based on an estimate of 10-year total CV risk determined by the FRS. Patients at high risk should be treated with statin therapy independent of baseline LDL-C, whereas healthy behaviour intervention alone may suffice for those with a low risk score. For individuals with a moderate risk score, recognition of cardiometabolic risk may justify managing the patient as if he or she were at high risk. The American Diabetes Association/American College of Cardiology consensus statement on lipoprotein management in patients with cardiometabolic risk suggests that individuals with an FRS of 10% to 19% be considered high risk if they have 2 or more cardiometabolic risk factors. The CHEP guidelines recommend statin therapy for individuals with systemic hypertension and 3 or more CV risk factors. However, the current CCS dyslipidemia guidelines state that a moderate-risk patient with apo B < 1.0 g/L does not require treatment with a statin just to achieve the apo B target of <0.8 g/L. In men aged >50 years and women aged >60 years with moderate FRS (10%-19%), hs-CRP > 2 mg/L identifies a group of patients who benefit from aggressive LDL-C reduction. Many of these patients will have cardiometabolic risk.

The CCS dyslipidemia guidelines recommend an apo B lipoprotein < 0.8 g/L as an alternative primary treatment target in high- and moderate-risk patients. In patients with cardiometabolic risk and relatively low baseline LDL-C, apo B is likely to be a more useful measurement than LDL-C. Apo B lipoprotein measurement is valuable in the identification of high CAD risk in individuals with cardiometabolic risk. Additional investigations may help to better stratify risk and may include measurement of hs-CRP, noninvasive imaging of the carotid arteries for atherosclerosis, measurement of the ankle-brachial index, and an assessment of cardiorespiratory fitness.

**What are the treatment goals of lipid therapy?**

Individuals with IGT have a risk of CAD close to that of people with diabetes. Consequently, there is justification to recommend
that they receive statin therapy to achieve LDL-C targets similar to those for patients with established diabetes. The current CCS dyslipidemia guidelines recommend a >50% reduction of LDL-C or target level of <2.0 mmol/L in subjects considered to be at high risk. Similar treatment goals should be sought in the patient with a moderate FRS and multiple cardiometabolic risk factors. In subjects with isolated IFG (ie, with a known normal 2-hour 75-g oral glucose tolerance test value), CAD risk is lower than in those with IGT. In the absence of multiple cardiometabolic risk factors, these subjects should likely be managed according to their FRS, LDL-C, or apo B levels. Apo B may be helpful in achieving an optimal reduction of cardiometabolic risk, especially in individuals with hypertriglyceridemia and low HDL-C. (See Tables 7 and 8.)

Can we reduce residual risk by managing other lipid targets? There is a large residual risk for patients at high risk for CVD, despite LDL-C reduction with high-dose statins. Most patients with cardiometabolic risk have an acquired combined hyperlipidemia, associated with increased TGs, a modest increase in LDL-C, and low HDL-C. LDL particle numbers are increased, as reflected by the increased levels of apo B_{100}.

Beyond LDL-C lowering, other strategies that might reduce the residual risk include the optional secondary targets discussed in the most recent CCS dyslipidemia guidelines. These include reducing the total cholesterol–to–HDL-C ratio, hs-CRP, and TGs, although there are no clinical trial data to support such strategies. In the patient with diabetes, optimization of glycemic control 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 (ACCORD), 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 individuals with high TGs and/or low HDL-C, as had been shown in patients with the same lipid profile features in the Fenofibrate Intervention in Event Lowering in Diabetes (FIELD) trial, the Bezafibrate Infarction Prevention study, and the Veterans Affairs High-density Lipoprotein Trial. We await the results of ongoing clinical trials such as the Atherosclerosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides and Impact on Global Health Outcomes, the Treatment of HDL to Reduce the Incidence of Vascular Events, and the Study of RO4607381 [dalteparin] in Stable Coronary Heart Disease Patients With Recent Acute Coronary Syndrome, which are assessing whether the addition of other second lipid-modifying agents to a statin will be associated with additional CV risk reduction.

Hypertension control

Over 30% of people with metabolic syndrome have systemic hypertension. In addition, approximately 20% of people with hypertension have IGT. These individuals are at higher risk of developing diabetes and CVD. Furthermore, chronic renal insufficiency (glomerular filtration rate < 60 mL per minute) is approximately 2.5 times more common in people with metabolic syndrome.

Who should receive antihypertensive treatment and to what goals? The CHEP guidelines recommend health behaviour changes for people at risk for developing hypertension, specifically physical exercise, weight reduction, maintenance of a healthy BMI and waist circumference, and moderation of alcohol and sodium intake. The CHEP guidelines recommend people with cardiometabolic risk should be treated to a BP < 140/90 mm Hg, unless they have diabetes or chronic kidney disease, in which case a lower target of <130/80 mm Hg should be used. Yet the recently reported Action to Control Cardiovascular Risk in Diabetes BP trial in patients with diabetes failed to show benefit of systolic BP lowering to 120 mm Hg compared with 140 mm Hg. (See Tables 7 and 8.)

Should specific antihypertensive agents be chosen or avoided in individuals with cardiometabolic risk? Clinical trials have not specifically evaluated BP lowering in individuals with cardiometabolic risk. However, RAAS inhibitors have been prospectively tested in individuals with prediabetes for the prevention of new-onset diabetes. In the Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research study, valsartan was shown to reduce the incidence of diabetes by 14% in individuals with IGT and heightened CV risk. In the Diabetes Reduction Assessment With Ramipril and Rosiglitazone Medication, ramipril was found to have a smaller, nonsignificant effect on the prevention of diabetes in individuals with either IFG or IGT. In a systematic overview of 3 large trials of ACE inhibition in individuals with CVD, but without diabetes, a reduction in diabetes of similar magnitude was observed. Therefore, in individuals with cardiometabolic risk associated with dysglycemia, it may be advisable to use antihypertensive drugs that may be associated with improvement of glucose metabolism (ie, RAAS inhibitors) or agents that are metabolically neutral (ie, calcium channel blockers [CCBs]). Thiazide diuretics are associated with an increased risk for development of new diabetes. In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, chlorthalidone treatment was associated with a greater incidence of new diabetes than in patients treated with either amlodipine or lisinopril. Yet prevention of MI was similar with all 3 agents during the study’s relatively short period of observation. In a long-term cohort study of newly treated hypertensive patients, with follow-up 1 to 16 years (median, 6 years), the development of new diabetes was associated with a risk of CV events that was similar to that of individuals with previously known diabetes. 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 and improved CV outcomes related to differences in blood glucose level and body weight. Consequently, in patients with cardiometabolic risk, it may be preferable to use antihypertensive therapies that are metabolically neutral (ie, CCBs). In patients with cardiometabolic risk who require BP lowering with multiple agents, combining an ACE inhibitor and a CCB may be preferred to combining an ACE inhibitor and a diuretic.

How can the risk for diabetes be reduced in the patient with cardiometabolic risk?

Individuals with cardiometabolic risk are at a substantially greater risk of developing type 2 diabetes, with its associated incremental risks for CVD and renal disease. For patients with IFG, IGT or metabolic syndrome, health behaviour modification with weight loss and increased physical activity are the...
most effective\textsuperscript{210} (See the section titled Health Behaviour Interventions to Reduce Cardiometabolic Risk). While health behaviour change is most effective, metformin,\textsuperscript{126} acarbose,\textsuperscript{131} rosiglitazone,\textsuperscript{132} pioglitazone,\textsuperscript{134} combination therapy with metformin and rosiglitazone,\textsuperscript{133} and orlistat\textsuperscript{135} have all been shown to reduce progression to type 2 diabetes. In the Diabetes Prevention Program, metformin reduced progression from IGT to diabetes\textsuperscript{26} Rosiglitazone was shown in the Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication trial to reduce the development of diabetes in subjects with either IGT or IFG, yet the study was not powered to examine CV outcomes.\textsuperscript{132} The Study to Prevent Non-Insulin-Dependent Diabetes suggested that a reduction of the incidence of new diabetes with acarbose was associated with a reduction of CV events.\textsuperscript{131} In the Xenical in the Prevention of Diabetes in Obese Subjects study, orlistat treatment was associated with a reduction in weight and in the incidence of diabetes.\textsuperscript{135} The recently published Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research showed that valsartan exerted a modest reduction in the development of new diabetes (hazard ratio, 0.86; 95% CI, 0.8-0.92; \( P < .001 \)) in patients with both IGT and either CVD or CV risk factors.\textsuperscript{204} However, neither valsartan\textsuperscript{212} nor the antihyperglycemic agent nateglinide\textsuperscript{204} had any impact on CV events (CV death, nonfatal MI, nonfatal stroke, hospitalization for unstable angina, heart failure, or arterial revascularization; see Tables 7 and 8). While health behaviour modifications are the preferred strategy to prevent diabetes, if pharmacologic interventions are added to health behaviour, metformin is indicated as first-line therapy, based on its efficacy, safety, and cost.

**Antithrombotic therapy**

Enhanced platelet activity plays a role in the increased risk of atherothrombosis in individuals with metabolic syndrome. Antithrombotic therapy with acetylsalicylic acid (ASA) is an established treatment for the secondary prevention of coronary events in high-risk patients with acute or chronic CAD.\textsuperscript{215} However, a meta-analysis of ASA trials for the primary prevention of CAD showed no mortality benefit, a small absolute reduction of CAD in men (8/1000 treated over 6.4 years), but not women, and a reduction of stroke in women (3/1000), but not men.\textsuperscript{214} For individuals with hypertension and increased vascular risk with metabolic syndrome or dysglycemia, the Hypertension Optimal Treatment trial\textsuperscript{215} also showed a very small absolute reduction (0.16%) using ASA in patients with multiple CV risk factors and hypertension, once BP is adequately controlled. Furthermore, for patients with diabetes and no clinical evidence of vascular disease, a recent meta-analysis failed to show evidence that ASA provides any protective benefit.\textsuperscript{216} Hence, the benefits of ASA for primary prevention are very small and offset by bleeding risk, even when used in patients with risk factors such as diabetes.

**Should patients with cardiometabolic risk receive ASA?** Although a recent US Preventive Services Task Force Recommendation Statement\textsuperscript{217} recommends ASA for primary prevention in men aged 45 to 79 years and women aged 55 to 79 years, current clinical trial evidence is not supportive of this advice. In the absence of a clinical history of CAD (MI or angina), stroke or peripheral arterial disease, or vascular imaging showing atherosclerosis, there is no evidence to support the use of ASA with cardiometabolic risk.

**Antithrombotic therapy**

Clinician counselling with pharmacologic assistance in a motivated patient is most likely to result in long-term abstinence than either strategy alone. Nicotine replacement (gum or patch), bupropion, and varenicline are pharmacologic agents that have been shown to improve the success of smoking cessation by successfully treating the addiction component of smoking.\textsuperscript{219}

**Which patients should receive pharmacologic agents to help increase the success of smoking cessation?** All patients who are motivated to stop smoking should be offered both medication and counselling, as well as follow-up contacts to prevent relapse.\textsuperscript{220} Combinations of medications should be considered. Motivated patients should be managed through a multidisciplinary smoking cessation program when one is available locally.

**Summary**

Vascular protective measures are essential for all patients with cardiometabolic risk.

**Health behaviour modification:** As discussed in the section titled Health Behaviour Interventions to Reduce Cardiometabolic Risk.

**Optimizing BP levels:** In hypertensive patients, BP control should be achieved. In individuals with cardiometabolic risk associated with dysglycemia, it may be advisable to use antihypertensive agents associated with improved glucose metabolism or agents that are metabolically neutral.

**Optimizing lipid levels:** In patients with cardiometabolic risk with a moderate or high FRS, treatment should be initiated with a statin to reduce 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 <0.80 g/L in high-risk and moderate-risk individuals.

**Optimizing blood glucose levels, preventing progression to diabetes and managing hyperglycemia:** In patients with cardiometabolic risk, weight loss and increased physical activity are recommended to reduce risk. Pharmacotherapy can also be considered as per the Canadian Diabetes Association 2008 guidelines.

**Antithrombotic therapy:** The benefits of ASA 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. In patients with cardiometabolic risk, in the absence of a clinical history of coronary heart disease (MI or angina), stroke, or peripheral vascular disease, or of vascular imaging showing atherosclerosis, there is no evidence to support the use of ASA.

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

### Cardiometabolic Risk in Susceptible Canadian Populations

**M. Gupta, S. Anand, C.-M. Chow, S.B. Harris, S. Qaadri, and H. Teoh**

**How do ethnicity and culture impact on cardiometabolic risk?**

Canada is one of the world’s most ethnically diverse countries. It has been recognized that ethnicity may impact on health outcomes, including the risk for cardiometabolic diseases. Accordingly, in order to appropriately assess and screen individuals in Canada’s diverse patient populations, Canadian health care professionals must be aware that risk factors vary in frequency among certain ethnic populations. This section focuses on the prevalence of cardiometabolic risk factors in 3 of Canada’s susceptible populations: South Asians, Chinese, and Aboriginals. It is important to note that research and data are lacking for certain susceptible populations entirely, and for risk factors in a given population. In Canada, this particularly applies to the Afro-Caribbean population. As there are no agreed-on terms in the literature to describe each population, the terms used in this section reflect the language used by the authors of the relevant studies.

CVD rates vary considerably among Canadians of differing ethnic origins, but the reasons for this variation have not been fully elucidated. For example, the Study of Health Assessment and Risk in Ethnic Groups (SHARE) found differences in the prevalence of conventional and emerging risk factors among South Asians, Chinese, and individuals whose ancestors originated from Europe, all residing in Canada, but this variation did not fully explain the higher rates of CVD noted among South Asians. It is important that SHARE suggested that findings from studies carried out in European populations cannot be fully extrapolated to other ethnocultural populations.

**Table 14. Cultural and clinical considerations regarding cardiometabolic risk and assessment in select at-risk populations**

<table>
<thead>
<tr>
<th>Population (originating from)</th>
<th>Cultural considerations</th>
<th>Clinical considerations</th>
</tr>
</thead>
</table>
| South Asian (India, Pakistan, Sri Lanka, Bangladesh, and Nepal) | An extremely heterogeneous population, with wide variations in approaches to health, health behaviour, diet, and tobacco consumption224 | **BMI and WC:**  
  ● Increased cardiometabolic risk at BMI or WC levels traditionally considered “normal.”  
  ● Use ethnic-specific WC and BMI cutoffs (see Table 1)  
  **BP:**  
  ● Three times more likely to have HT than people of European descent226  
  **Lipids:**  
  ● Higher LDL-C than Europeans and Chinese222  
  **Diabetes:**  
  ● High prevalence of diabetes98 |
| Chinese (Mainland China, Hong Kong, Malaysia, Singapore, and Taiwan) | Recent change in the demographics of the immigrants: now from mainland China and speaking mainly Mandarin (vs traditional immigration from Cantonese-speaking regions of southern China, namely Hong Kong)222 | **BMI and WC:**  
  ● Increased cardiometabolic risk at BMI or WC levels traditionally considered “normal”  
  ● Use ethnic-specific WC and BMI cutoffs223 |
| Aboriginal (Canada) | Rapid cultural transition over the past 2 or 3 generations, highlighted by a shift away from traditional health behaviours toward more sedentary living and Western diets, has translated into a heightened risk for chronic disease | **BMI and WC:**  
  ● With high rates of obesity, focus on physical activity and other healthy behaviours.  
  **Diabetes:**  
  ● High rates of diabetes  
  ● Screening for diabetes should be considered every 1 to 2 years in individuals with more than 1 risk factor98  
  ● Individuals with normal results, but with risk factors, should receive health behaviour counselling  
  ● Annual OGTT testing should be encouraged in individuals with IGT98  
  **Smoking:**  
  ● Among the highest rates of smoking in the world226  
  ● Smoking prevention and cessation should be a priority |

BMI, body mass index; BP, blood pressure; HT, hypertension; IGT, impaired glucose tolerance; LDL-C, low-density lipoprotein cholesterol; OGTT, oral glucose tolerance test; WC, waist circumference.
tively, 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 lack of physical activity. The proportional contribution of these risk factors to risk of first MI was consistent across all ethnic groups.22 These findings stress the importance of addressing these risk factors (through prevention and treatment) in all populations, regardless of ethnic origin.

**What is known about cardiometabolic risk in South Asians?**

South Asian ethnicity has been suggested to be an independent risk factor for CVD.222,226 People of South Asian origin are at increased risk for premature CAD,227 with an approximately 3- to 5-fold increased risk for MI and CV death compared with other ethnic groups.228 In addition, in an analysis of age-standardized mortality in Canada over 15 years, South Asians had the highest CAD mortality compared with individuals of European or Chinese descent.229

In the SHARE study, South Asians had the highest prevalence of CVD and an increased prevalence of glucose intolerance and dyslipidemia, as well as more abnormalities of novel risk factors (such as increased fibrinogen, homocysteine, lipoprotein (a), and plasminogen activator inhibitor-1).222 Compared with matched controls of various ethnic descents, South Asian Canadians have been found to present to the hospital later in the course of acute MI; be more likely to have an anterior infarction226; be younger at the first hospitalization for heart failure226,231; and at the time of catheterization,232 have more significant left main, multivessel, and distal CAD;232 have poorer outcomes and survival from coronary artery bypass surgery (CABG)233; have CAD at lower BMI (actually within the “reference range”)226,230; be more likely to have diabetes234; and be more likely to have evidence of CAD, even in the absence of symptoms or clinical findings.235 A recent analysis of CV risk profiles of major ethnic groups in Ontario demonstrated that South Asians have a higher prevalence of heart disease and strokes than does the white population.235

In the INTERHEART study,231 the average age of first MI in South Asians was approximately 10 years younger than in the rest of the study population. However, after adjusting for the major INTERHEART risk factors, particularly smoking, high ratio of apo B100 to apo A1, hypertension, and diabetes, this age difference became insignificant, suggesting that South Asians do not necessarily have “unexplained CAD risk factors”; rather they accrue known risk factors at a younger age, thus explaining the premature onset of CAD. Possible explanations for South Asians’ development of risk factors at younger ages include genetic predisposition, unique health behaviours, and/or an interaction between the two.

Compared with other populations, South Asians have been found to have higher LDL-C, lower HDL-C, and higher TGs.222,232,234 South Asian men have been shown to have higher concentrations of small HDL particles (the cardioprotective properties of HDL are likely restricted to the larger particles), and some studies have shown higher levels of small, dense LDL particles, which may be more atherogenic.222,234

In a recent Ontario survey on the prevalence and control of hypertension, South Asians were 3 times more likely than white people to have hypertension.236 Ontario data on CV risk factors also revealed that smoking and obesity are less prevalent in South Asian than in white populations.237

The prevalence of diabetes is uniformly higher among South Asians than in most comparative populations. In Ontario, compared with immigrants from western Europe and North America, those from South Asia have the highest prevalence of diabetes, followed by those from Latin America, the Caribbean, and sub-Saharan Africa.237 In SHARE, South Asians had almost 3 times the prevalence of treated diabetes as people of European descent. Testing with a 2-hour oral glucose tolerance test revealed that one-third of South Asians without known diabetes had either IGT or type 2 diabetes (despite having a lower BMI compared with people of European descent).222 A well-documented pattern of type 2 diabetes or glucose intolerance, often associated with reduced HDL-C and increased TGs, in South Asians suggests that insulin resistance may partially explain the excess CAD risk in this population.234

When obesity is defined by standard criteria, such as BMI ≥ 30 kg/m², South Asians have a low prevalence of obesity compared with other populations.228 However, abdominal obesity, as suggested by increased waist circumference, seems to be highly prevalent in this population and is independently associated with both diabetes and CVD. Thus, South Asians may exhibit considerable cardiometabolic risk at BMI or waist circumference levels traditionally considered “normal”.238 Accordingly, lower BMI and waist circumference thresholds have been advocated in South Asians. In fact, some studies suggest that the ideal BMI in a South Asian individual may be between 19 and 21 kg/m².226

South Asians are more likely to have visceral fat across the BMI spectrum. This is accompanied by a higher degree of insulin resistance for the same BMI, even in individuals who are not obese.225,234 The hyperinsulinemia that accompanies insulin resistance is associated with premature CAD. South Asians, therefore, appear to have higher CAD risk at lower BMI compared with European populations. Accordingly, the World Health Organization has recommended lower BMI cutoffs for overweight (23 kg/m²) and obesity (25 kg/m²) in all Asians, including South Asians. The increased prevalence of abdominal obesity, metabolic syndrome, glucose intolerance, or a combination may mediate the excess CAD risk. Furthermore, South Asians have the least favourable adipokine profile, and like the Aboriginal people, they display a greater increase in insulin resistance with decreasing levels of adiponectin.239

**What is known about cardiometabolic risk in Chinese?**

Lipid levels in general are similar between Chinese and Europeans, but Chinese are more susceptible to the low HDL-C associated with metabolic syndrome and insulin resistance.222 Noteworthy is the high prevalence of dyslipidemia at low BMI values among Chinese adults from Singapore223 and Taiwan.241

Hypertension is the leading preventable risk factor for CVD and all-cause mortality in the developing world, and there is a strong linear association between BP levels and CVD in the Chinese.242 Chinese seem to be prone to elevated BP, with the risk increasing at a BMI of about 23 kg/m².243 In the Canadian SHARE study, the Chinese group had the highest rate of hypertension requiring medication.222 In an Ontario BP survey, East Asians, a heterogeneous ethnic group including Chinese,
CVD compared with the white population.235

In the SHARE study, if subjects with diabetes at baseline (2.6%) were excluded, the prevalence of newly diagnosed IGT or diabetes in the Chinese was 20%, compared with 18% of Europeans and 28% of South Asians.222 This is an important finding, as the Chinese had significantly lower BMI than did Europeans, yet had intermediate rates of dysglycemia.

For the same BMI, Chinese persons have been shown to have a higher percentage of body fat than white people do,244,245 which may explain the high prevalence of CVD risk factors at low BMI and waist-to-hip ratios, as well as the high morbidity and mortality from CVD even in the presence of low population-mean BMI and obesity rates. In an analysis of SHARE,225 among Chinese with a BMI > 23 kg/m², BP, glucose, and lipids became abnormal. Hence, universal BMI cutoff points are not appropriate,244,245 and the use of values extrapolated from those of white people may significantly underestimate risk.

In INTERHEART, the Chinese had a more favourable lipid profile than did people in other regions of the world. The associations between first MI and diabetes, depression, and stress were stronger for the Chinese than for other participants, whereas the association between first MI and abdominal obesity was significantly lower.246

Identifying those with hypoadiponectinemia and elevated waist circumference has been shown to increase the sensitivity of identifying Chinese subjects at particular risk of glucose intolerance and clustering of other risk factors.247,248 It is, however, recognized that the measurement of adiponectin cannot be readily performed at the present time.

What is known about cardiometabolic risk in Aboriginal people?

Compared with Canadians of European descent, Canada’s Aboriginal people have a higher prevalence of carotid atherosclerosis and CVD and significantly higher rates of smoking, glucose intolerance, obesity, and abdominal obesity.222,249,251 In one community, a tripling in admission rates for ischemic heart disease was observed during a 15-year period.252

Despite a rich variation in location, language, history, and culture, increased rates of type 2 diabetes in comparison with the nonindigenous general population seem to be a shared phenomenon.253 Type 2 diabetes has reached epidemic proportions among Canadian Aboriginals/First Nations peoples. The age-adjusted national prevalence is 2.5 to 5 times higher in First Nations people than in the general population,254,255 with prevalence rates as high as 26% in some communities.256 First Nations peoples are also diagnosed with type 2 diabetes at a much younger age.254,255 Recent data indicate that the incidence of type 2 diabetes is increasing among children and youth aged <18 years and disproportionately among Aboriginal youth.257

In the 2004 Canadian Community Health Survey, the prevalence of obesity in adults was 37.8% among Aboriginals, compared with 22.6% in non-Aboriginals, and in children and youth, the respective rates were 15.8% vs 8.2%.258 In the Canadian First Nations Diabetes Clinical Management Epidemiologic (CIRCLE) study carried out in partnership with 19 First Nations communities across Canada, 25.7% of adults were obese (BMI 30.0–34.9 kg/m²), and 30.3% were classified as morbidly obese (BMI ≥ 35.0 kg/m²).259

A number of other factors may contribute to the high rates of disease. These include genetic susceptibility, high-fat and high-glycemic-load diets, low levels of physical activity (partly due to environments not conducive to physical activity), smoking, geographic isolation, and remoteness (leading to inadequate access to care). In addition, social factors such as high rates of poverty, inferior health care and social service infrastructure, educational disadvantage, and high unemployment rates may be implicated.259-262 Aboriginal peoples in Canada are more socially disadvantaged than populations of European, South Asian, or Chinese ancestry.263 Worldwide, Aboriginal peoples have unemployment and poverty rates almost 2 to 4 times higher than national benchmarks.264 In Canada, diabetes rates have been shown to be inversely correlated with household income level.265 For any given income level, Aboriginal people have a higher prevalence of risk factors and CVD than do Europeans.266

Aboriginal Canadians have among the highest rates of smoking in the world (First Nations, 56%; Métis, 57%; Inuit, 72%).267 In the Ojii-Cree community of Sandy Lake, 50% of the participants overall and 82% of the adolescent participants (aged 15-19 years) were current smokers. An independent dose-response relation was found between current smoking exposure and both traditional (systolic BP) and nontraditional (homocysteine level) CVD risk factors. The relationship between smoking and increased CV risk at an early age may be a contributing factor to the high prevalence of CVD in this population.267 Together, these factors result in the marginalization of Aboriginal peoples and may produce stressful environments that impact health and cardiometabolic disease through both psychosocial and behavioural pathways.268

What do we know about cardiometabolic risk in Afro-Caribbeans?

Recent Canadian Census data indicate that of immigrants to Canada from 2001 to 2006, 11% were from Central or South America, and 10.6% were from Africa. Unfortunately, there is a lack of studies among Afro-Caribbeans in Canada. Although there is a wider American literature on health service use and outcomes in African Americans, it is unknown whether findings in that population would apply to the Canadian Afro-Caribbean population. Canadian guidelines include African descent as a risk factor for type 2 diabetes.269 In addition, an Ontario BP survey found that black people (primarily of Caribbean origin) had the highest prevalence of hypertension among the 4 ethnic groups studied, with a 3.3-fold increase in the prevalence of hypertension compared with the reference white population. In addition, they developed hypertension at a much earlier age; by age 60, 50% of this population had hypertension.270

A recent Ontario study revealed a paradox among Ontarians of black ethnicity: While they had least favourable overall CV risk profile compared with Ontarians of white, Chinese, or South Asian ethnicity, they had a relatively low prevalence of heart disease.235
What is known about emerging risk factors in susceptible populations?

Several studies have shown higher levels of hs-CRP in South Asians compared with Caucasians, a difference that persists even after adjusting for total body fat and waist circumference, suggesting that South Asians may have an underlying proinflammatory state linked to excess visceral adiposity that may contribute to their increased risk of diabetes and CAD. CRP levels have been shown to vary significantly among ethnic populations and to be influenced by the differences in metabolic factors in these populations. However, prospective validation of the predictive value of CRP for CVD among non-Europid populations is needed. In addition, it has been shown that the nonfasting ratio of apo B to apo A1 is superior to any of the cholesterol ratios for estimation of the risk of acute MI in all ethnic groups, in both sexes and at all ages. However, this test is not routinely available in Canada, and there are no current guideline recommendations regarding this ratio, either for screening or as a target of therapy. Given that South Asians have proportionately more visceral fat (across the BMI either for screening or as a target of therapy. Given that South Asians have proportionately more visceral fat (across the BMI range) than do other populations, altered levels of adipokines (adiponectin, resistin, and leptin) have been implicated in the pathogenesis of insulin resistance in this population.

Many emerging risk markers are under investigation and may vary among ethnic groups, but none has yet been shown to substantially aid in risk stratification beyond traditional risk factors, nor has any been shown to specifically improve risk stratification in particular ethnic groups. Noninvasive imaging of atherosclerosis, such as with carotid intima-media thickness measurement, has potential screening utility in the future, but further studies are required. The SHARE study revealed that carotid atherosclerosis in healthy middle-aged Canadians was fairly common (23% prevalence) and occurred with similar prevalence among white Europeans (25%), Chinese (24%), Aboriginals (20%), and South Asians (22%).

Does socioeconomic status impact on cardiometabolic risk?

Anand and colleagues studied the relationship between socioeconomic status, CV risk factors, and CVD among men and women from diverse ethnic populations. The most socially disadvantaged were more likely to be older, women, smokers, and have higher body weight, abdominal obesity, glucose, and inflammatory marker elevation compared with less socially disadvantaged individuals. Indeed, for every 1-point increase in the index used to calculate social disadvantage, the relative increase in CVD was 25% (range, 6%-47%). People of European origin were the least socially disadvantaged, compared with Aboriginal people (who were the most socially disadvantaged), with Chinese and South Asians having intermediate levels of social disadvantage. Independent of age, social disadvantage is associated with an increase in some, but not all, CV risk factors and has been shown to be a significant predictor of CVD.

The highest rates of diabetes are seen in the lower-income quintiles. In the 1998-1999 National Population Health Survey, 21.4% of people with diabetes reported low income (vs 12.8% in the general population), and 42.7% reported not finishing secondary school (vs 22.5% in the general population). People in lower income brackets and with fewer years of formal education also reported higher rates of smoking, less physical activity, and higher rates of overweight. Smoking prevalence is twice as high for the lowest family-income category as for the highest (37% vs 20% for men and 30% vs 16% for women).

Household food insecurity has also been shown to be associated with poorer health. The prevalence of household food insecurity is higher among Canadians with diabetes and is associated with an increased likelihood of unhealthy behaviours that would impact on cardiometabolic risk (including physical inactivity, lower fruit and vegetable consumption, and current smoking). Research in the United States has demonstrated the association between food insecurity among low-income individuals and hypertension and hyperlipidemia.

Due to the paucity of Canadian research on the impact and implications of low socioeconomic status on cardiometabolic risk, recommendations on specific management of this population cannot be made. More research on the social determinants of health, specifically in the area of cardiometabolic diseases, will help clarify therapeutic strategies and the health policies needed to minimize risk in this population.

Therapeutic implications

Traditional risk factors explain the majority of CV events in all populations, including the specific populations discussed in this chapter. Thus, health behaviour 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 (see the section titled Health Behaviour Interventions to Reduce Cardiovascular Risk and the section titled Pharmacologic and Surgical Interventions to Reduce Cardiovascular Risk).

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. 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 among ethnic groups may be attributable to differences in pharmacokinetic and pharmacodynamic effects or to polymorphisms of genes critical to drug metabolism. Asians have historically been considered to be more responsive than white populations to the lipid-lowering effects of statins. As such, Health Canada and the US Food and Drug Administration recommend lower starting doses of certain statins in Asian patients. Recent data, however, suggest that people of South Asian origin derive similar lipid effects from atorvastatin and simvastatin as white populations and that dose adjustment in South Asians may not be necessary.

Summary and implications

Evidence-based prevention strategies and therapies recommended by major national guidelines should be optimally employed in the management of cardiometabolic risk in all populations, including increased and regular physical activity to prevent weight gain or promote weight loss, healthy dietary patterns, and as per the suggestions outlined earlier in this document (see the section titled Health Behaviour Interventions to Reduce Cardiovascular Risk and the section titled Pharmacologic and Surgical Interventions to Reduce Cardiovascular Risk).
practices, control of risk factors with therapies proven in randomized trials, and aggressive secondary prevention strategies when vascular disease is established. However, 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, should reflect the ethnocultural representation, should be culturally sensitive, and when possible should be delivered in the patient’s language of choice.

Research is needed to develop reference data that are based on health-related criteria or outcomes (rather than being merely representative of the population), and population-based research is needed to help establish ethnic-specific cutoff values for waist circumference with sensitivity and specificity to discriminate clinical events. It is important to note that to our knowledge there are no data on youth in Canada’s ethnocultural communities—a situation that must be addressed if successful prevention strategies are to be implemented.

In conclusion, Canadian health care professionals must be aware of ethnicity-related risk factors in order to appropriately assess and screen individuals in their diverse patient populations. As the relationship between percentage body fat and BMI is ethnic specific, ethnic-specific cutoff for measurements of overweight and central adiposity are recommended. Community-based prevention and management programs should be developed and delivered in partnership with target communities, should reflect the ethnocultural representation, should be culturally sensitive, and when possible should be delivered in the patient’s language of choice. Evidence-based prevention strategies and therapies recommended by major national guidelines should be optimally employed in the management of cardiometabolic risk in all populations.

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