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## Comprehensive Cardiovascular Risk Reduction and Cardiac Rehabilitation in Diabetes and the Metabolic Syndrome

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### Abstract

The epidemic of obesity has contributed to a growing burden of metabolic syndrome (MetS) and diabetes mellitus (DM) worldwide. MetS is defined as central obesity along with associated factors such as hypertriglyceridemia, low high-density lipoprotein cholesterol, hyperglycemia, and hypertension. MetS and DM are associated with significant cardiovascular morbidity and mortality. Healthy behavioural modification is the cornerstone for reducing the atherosclerotic cardiovascular disease burden in this population. Comprehensive, multi-disciplinary cardiac rehabilitation (CR) programs reduce mortality and hospitalizations in patients with MetS and DM. Despite this benefit, patients with MetS and DM are less likely to attend and complete CR because of numerous barriers. Implementation of innovative CR delivery models might improve utilization of CR and cardiovascular outcomes in this high-risk population.

### Abstract

L'épidémie d'obésité a contribué au fardeau croissant du syndrome métabolique (SMét) et du diabète dans le monde entier. Le SMét est défini par la présence de l'obésité abdominale ainsi que des facteurs qui y sont associés tels que l'hypertriglycéridémie, le faible taux de cholestérol à lipoprotéines de haute densité, l'hyperglycémie et l'hypertension. Le SMét et le diabète sont associés à une morbidité et une mortalité cardiovasculaires significatives. La modification des comportements en matière de santé est la pierre angulaire de la réduction du fardeau de la maladie cardiovasculaire athérosclérotique dans cette population. Les programmes multidisciplinaires exhaustifs de réadaptation cardiaque (RC) réduisent la mortalité et les hospitalisations chez les patients atteints du SMét et du diabète. En dépit de ces avantages, les patients atteints du SMét et du diabète sont moins susceptibles de participer et de compléter la RC en raison des nombreux obstacles. La mise en œuvre de modèles novateurs de prestation de programmes de RC améliorerait la participation à la RC et les issues cardiovasculaires de cette population à risque élevé.

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Cardiovascular (CV) disease (CVD) is the leading cause of mortality worldwide.<sup>1</sup> An epidemic of obesity has contributed to an increasing prevalence of CVD risk factors such as metabolic syndrome (MetS) and diabetes mellitus (DM). MetS is defined as a clustering of interrelated metabolic factors that together represent a multiplex CV risk factor.<sup>2</sup> According to the harmonized definition, MetS is classified as central obesity (see Table 1 for criteria) with associated factors such as hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), hyperglycemia, and hypertension (Table 2).<sup>3</sup> Waist circumference thresholds for abdominal obesity have been shown to vary according to region and ethnicity. The International Diabetes Foundation (IDF) defines this similarly with 2 important exceptions: that (1) abdominal obesity is central to MetS; and thus, (2) abdominal obesity plus 2 of the other remaining 4 criteria must be met. Additionally, because of the variations in waist measurements, the IDF has developed alternative waist circumference thresholds for defining abdominal obesity (Table 1). Multiple landmark trials have used obesity cut points from the National Cholesterol Education Program and IDF for the MetS. The IDF criteria were found to be slightly more sensitive for the diagnosis of MetS (13.3% vs 10.4%) than the National Cholesterol Education Program criteria in a head-to-head comparison.<sup>4</sup>

The prevalence of obesity and associated MetS has increased to epidemic proportions globally. According to the World Health Organization (WHO), the rate of obesity has doubled since 1980, with 600 million people, or 13% of the global population, meeting criteria for obesity.<sup>5</sup> A similar trend is observed in the Canadian population. Results from the Canadian Community Health Survey from 2010 to 2014 show that the prevalence of obesity has increased from 38.1% to 40%.<sup>6,7</sup> The relationship between obesity and MetS was illustrated in the National Health and Nutritional Examination Survey (NHANES) III study, which identified the presence of MetS in 5% of normal weight, 22% of overweight, and 60% of obese individuals.<sup>9</sup> This is largely attributed to an increase in poor nutrition, sedentary health behaviours, and the relative aging of populations.<sup>10</sup> MetS affected approximately 22.9% of adults (20 years of age and older) in the United States in 2010 and 25.5% of the overall population in 1999.<sup>11</sup> This favourable trend is attributed to a decrease in hypertriglyceridemia and hypertension because of improved medical management, despite waist circumference and hyperglycemia becoming increasingly widespread over the same period of time.<sup>11</sup> Despite this encouraging trend, MetS remains a significant cause of morbidity and mortality worldwide.

Socioeconomic status has been shown to have an influence on one's likelihood of being diagnosed with MetS in Canada.<sup>12,13</sup> Along with MetS, the prevalence of DM continues to increase in epidemic proportions. Thirty million people worldwide were estimated to have DM in 1985, and this figure is projected to approach 350 million by 2050.<sup>14</sup> As of 2009, there were 2.4 million people (6.8%) with DM living in Canada, with 7.2% of men and 6.4% of Canadian women having DM.<sup>15</sup> The Canadian Diabetes Association has estimated that the 2015 prevalence of DM in Canada had climbed to 9.3% of the population and would continue to climb to 12.1% by the year 2025.<sup>16</sup>

## Complications and Consequences

### Consequences of obesity

Excess adiposity and obesity are associated with the development of MetS and DM. Body mass index (BMI) is a population-based estimate of body fat, and higher BMIs are associated with a greater incidence of diseases related to obesity. An individual with a BMI of 26 compared with another with a BMI of < 21 has a twofold increased risk of coronary artery disease (CAD) among women and a 1.5-fold increase among men. The association between BMI and DM is even more profound, with a fourfold increased risk of developing DM among men with a BMI of 26 and an eightfold risk in women of the same BMI.<sup>17</sup>

BMI is frequently used in epidemiologic studies because of its simplicity and convenience. There are, however, several limitations in using BMI as an assessment for body fat and CV risk such as the inability to differentiate fat mass from lean mass.<sup>17</sup> The distribution of body fat is another CV risk factor not adequately measured using BMI alone. Visceral adipose tissue disproportionately affects metabolic risk but is indistinguishable from subcutaneous adipose tissue using BMI.<sup>18</sup> Visceral adipose tissue is associated with increased bio-markers of insulin resistance, dyslipidemia, and inflammation. Visceral adiposity causes many pathological metabolic changes, including increasing systemic levels of cytokines, increasing the liver's resistance to endogenous insulin, reducing HDL-C levels, and reducing the ability of the liver to synthesize very low-density lipoprotein.<sup>19</sup> These abnormal forms of lipid storage can result in risks similar to those of excessive lipid production or storage.<sup>20</sup> In contrast, subcutaneous adipose tissue has a more benign phenotype, which is less associated with dyslipidemia or atherosclerosis.<sup>18</sup> Because of these findings, measures of fat distribution, such as waist circumference and waist-to-hip ratio, are more specific to identify risk.<sup>3,18</sup>

Although excess body fat is an accepted risk factor for CVD, the mechanisms driving this association are still under investigation. Adipose tissue is actively involved in lipid storage but also functions as a metabolically-regulated endocrine organ.<sup>21,22</sup> Fat secretes cytokines and other proteins, collectively called adipokines, the dysregulation of which is theorized to contribute to a proinflammatory state.<sup>21</sup>

Excessive fat increases an individual's production of inflammatory proteins including interleukin (IL)-6, tumour necrosis factor- $\alpha$ , leptin, resistin, angiotensinogen, and C-reactive protein (CRP), leading to a chronic low-grade inflammatory state that directly promotes atherogenesis. Adipokines also regulate other processes known to contribute to atherosclerosis, such as insulin resistance, hypertension, and endothelial dysfunction.<sup>21,22</sup> Tumour necrosis factor- $\alpha$ , for example, is an adipokine that directly upregulates inflammatory changes in the vascular tissue, promoting insulin resistance through inhibition of the insulin receptor signalling pathway.<sup>21,22</sup>

### Complications of the MetS

MetS adversely affects CV outcomes through a combination of atherogenic dyslipidemia and dysglycemia. These factors result from the proinflammatory state associated with obesity, hypertension, and a prothrombotic state.<sup>23,24</sup> Individuals with at least 4 of 5 features

of MetS (Table 1) have a 3.7-fold increased risk of CAD at 5-year follow-up.<sup>25</sup> Long-term follow-up of individuals who met at least 3 criteria for MetS were reported to have a 4.2 times higher incidence of CAD.<sup>26</sup> A study of adults in the United States reported an increased adjusted risk of heart disease mortality (HR 2.02, CI 1.42-2.89), CVD mortality (HR 1.82, CI 1.40-2.37), and all-cause mortality (hazard ratio [HR], 1.40; 95% confidence interval [CI], 1.19-1.66) in individuals with MetS compared with those without MetS.<sup>27</sup> Importantly, the increased risk of mortality persisted in those with MetS, even in the absence of established DM.<sup>27</sup> A similar study of elderly subjects (aged 65-74 years) without DM reported increased coronary heart disease (CHD; HR, 1.58; 95% CI, 1.14-2.18), CVD (HR, 1.51; 95% CI, 1.17-1.93), and all-cause (HR, 1.21; 95% CI, 1.01-1.46) mortality in individuals with MetS, as defined by WHO criteria, after adjustment for age, sex, history of myocardial infarction (MI) and stroke, current smoking, alcohol consumption, leisure physical activity, and total cholesterol.<sup>28</sup> Furthermore, MetS also increases the adjusted risk for incident fatal or nonfatal stroke (HR, 1.57; 95% CI, 1.12-2.19) in nondiabetic individuals during a 14-year follow-up.<sup>29</sup>

### Complications of DM

The effect of DM on CVD is well established. Eighty percent of individuals with DM will have a significant adverse cardiac event that will lead to their death, compared with 30% of the nondiabetic population.<sup>30</sup> Diabetic individuals, adjusted for population age differences, have a relative risk of 1.7 for CV death, 1.8 for hospitalization because of MI, and are 1.5 times more likely to suffer a stroke.<sup>5,31-33</sup> More importantly, DM confers the highest lifetime risk (67% in men and 57% in women) of any risk factor for developing CHD, and diabetic individuals are at the highest risk for macrovascular complications.<sup>34</sup> This association is further compounded by the fact that metabolic risk factors for atherosclerotic CVD (ASCVD) are commonly found in individuals with DM.<sup>35</sup>

The chronic complications of DM affect a variety of organ systems and are responsible for most related morbidity and mortality of the disease. Chronic complications of DM can be divided into vascular and nonvascular, with risk of complications for both increasing with degree and duration of hyperglycemia.<sup>8</sup> Vascular complications can be further subdivided into micro- and macrovascular complications. Microvascular complications include retinopathy and macular edema, neuropathy, and diabetic nephropathy.<sup>36</sup> Macro-vascular complications include CAD, cerebrovascular disease, and peripheral vascular disease.<sup>31</sup>

### Population Health

Health promotion and disease prevention have increasingly been recognized as an important intervention to address the growing global ASCVD burden. A number of major organizations have launched initiatives focused on reducing the burden of CVD. Among these efforts is the American Heart Association (AHA) 2020 Impact Goal, which prioritizes improving CV health by 20% and decreasing mortality from CV disease and stroke by 20% by the year 2020.<sup>37</sup> This would be accomplished by increasing awareness and counselling on risk factors such as tobacco abuse, obesity, poor nutrition, hypertension, hyperlipidemia, and disordered glucose metabolism. Similarly, the “25by25” initiative by the WHO is a

global effort with the stated goal of decreasing premature mortality from CV events, stroke, and DM by 25% by the year 2025. The Public Health Agency of Canada has a similar initiative with the Canadian Diabetes Strategy, which focuses on increased surveillance, public education, and community-based programs.<sup>15</sup>

Because of the increasing prevalence of obesity and MetS, a cardiometabolic think tank convened in June 2014 with a focus on defining and implementing new patient care models to best manage patients with CV risk factors and MetS.<sup>38</sup> This consortium created an integrated care model focused on prevention and disease management, which among other changes in care delivery, included a shift in care from the clinic to the community.<sup>38</sup>

This care model defines subtypes of MetS, including vascular dominant, lipid dominant, insulin resistant dominant, and adiposity dominant, allowing clinicians to appreciate the substantial variability in end organ consequences with differing management schemes. The model includes a staging system of MetS that ranges from at risk (stage A) to evidence of end organ damage (stage D). These changes signify the heterogeneity of the disease and highlight the need for more specific and evidence-based management algorithms.<sup>38</sup>

With the promise of emerging technology in health care comes the issue of our increasing dependency on technology and its complicated role in the obesity epidemic. At present, much of our transportation infrastructure is centred on the automobile. Environmental engineering-based public health initiatives, such as constructing cyclist-friendly roadways and increasing green space, can be important interventions. According to a 2010 report from the US Centers for Disease Control and Prevention, only 50% of individuals 18 years of age and older were achieving federal guidelines for physical activity, with this number decreasing to 30% for individuals older than the age of 75 years.<sup>39</sup> Positive changes at a legislative level, such as mandatory calorie labelling in restaurants and banning hydrogenated fats, can help decrease the burden of CV morbidity and mortality.<sup>40,41</sup> These population health initiatives are important efforts to reduce the global burden of CVD.

## Healthy Behaviour Management

Healthy behavioural modification, specifically focused on diet and exercise, remains a cornerstone for reducing the risk of MetS, DM, and ASCVD.<sup>38</sup> The American College of Cardiology and AHA Lifestyle Workgroup published guidelines on behavioural management focused on reducing CV risk in 2013.<sup>42</sup>

### Dietary modification

There is strong evidence that shows that low-density lipo-protein cholesterol (LDL-C) and blood pressure reduction is achieved with a dietary pattern that emphasizes vegetables, fruits, whole grains, low-fat dairy, fish, poultry, legumes, and nontropical vegetable oils. These dietary patterns are best achieved with approaches such as Dietary Approaches to Stop Hypertension, AHA Diet, and US Department of Agriculture Food Pattern.<sup>42,43</sup> Several trials involving patients with MetS provided a head-to-head comparison, showing the superiority of the Mediterranean-style diet (MedSD) over low-carbohydrate and low-fat diets for reducing the risk of developing CVD.<sup>44–47</sup>

The MedSD has also shown benefit in reducing CV risk.<sup>48,49</sup> Similar to other heart-healthy dietary patterns, this approach emphasizes whole grains, fresh fruit, vegetables, legumes, and nuts, in addition to limiting consumption of red meat. Other distinctive features are moderate consumption of wine and fatty fish, such as salmon and mackerel, which are rich in omega-3 fatty acids. Extra virgin olive oil is another staple of Mediterranean cuisine and is the primary source of added fat in these diets.<sup>42,48</sup>

The MedSD is associated with risk reduction for ASCVD and MetS and is effective for prevention of CVD.<sup>48</sup> In the **Prevención con Dieta Mediterránea (PREDIMED)** trial, participants assigned a MedSD had a 30% reduction in major CV events compared with the low-fat control group.<sup>50</sup> Subsequent analyses of PREDIMED have supported previous observational studies<sup>51,52</sup> and randomized controlled trials and have concluded that the MedSD promotes metabolic improvement in DM and MetS.<sup>53</sup> Similar results were seen in a meta-analysis of 50 studies representing 523,906 subjects. The Lyon Diet Heart Study showed that starting MedSD after having an MI was associated with a decreased risk of recurrent MI and cardiac death by 72% at 4 years.<sup>54</sup> Other objective measures of health also improve with a MedSD, including a decrease in waist circumference, systolic blood pressure, diastolic blood pressure, and glucose by 0.42 cm, 2.35 mm Hg, 1.35 mm Hg, and 3.89 mg/dL, respectively, and an increase in HDL-C by 1.17 mg/dL.<sup>49</sup> Such positive dietary changes also reduce serum concentrations of proinflammatory proteins including CRP, IL-6, and IL-8.<sup>55</sup>

### Physical activity

Physical activity is another important component of a heart-healthy life. Regular physical activity is associated with an antiatherogenic, anti-inflammatory, anti-ischemic, and antiarrhythmic effect along with an improvement in ASCVD risk factors.<sup>56,57</sup> The AHA/American College of Cardiology Lifestyle Workgroup advises adults to engage in 40 minutes of moderate to vigorous aerobic activity 3-4 times per week.<sup>42</sup> This regimen decreased LDL-C by 3-6 mg/dL and systolic and diastolic blood pressure by 2-5 mm Hg and 1-4 mm Hg, respectively.<sup>42</sup>

Regular aerobic exercise also improves individual risk factors related to the MetS.<sup>58</sup> In the **Studies Targeting Risk Reduction Interventions through Defined Exercise (STRRIDE)** trial, 334 subjects were randomized into 1 of 3 eight-month exercise programs. All 3 interventions prevented accumulation of visceral fat and participants had statistically significant reductions in waist size.<sup>59</sup> Surprisingly, after analyzing the intensity of exercise across intervention groups, the trial showed that low-intensity exercise might actually be superior for metabolic health.<sup>58</sup> In addition, those who engaged in assigned aerobic activity had a 52% improvement in insulin sensitivity, which was sustained for as many as 14 days after the most recent aerobic activity session.<sup>60</sup>

Comprehensive CVD risk factor control remains suboptimal in diabetic individuals. A study by Wong et al. showed that despite an approximate 50% of diabetic patients being at goal for either hemoglobin (Hgb) A1c, blood pressure, or LDL-C, only 24% of these patients were at goal for all 3 risk factors.<sup>61</sup> The STENO-2 study showed that targeted and intensive multifactorial intervention reduces the development of CVD by 20%.<sup>62</sup> Systolic and

diastolic blood pressures were lower by 11 and 4 mm Hg, respectively, in the intensive intervention cohort. Fasting glucose control improved with an average reduction of 34 mg/dL and reduction in Hgb A1c by 0.5% in the intensive group. LDL-C was reduced by an average of 34 mg/dL. STENO-2 was able to provide a real world setting in which multiple parameters of risk reduction were discussed during patient encounters. Intensive pharmacologic therapy, including antihypertensive and antilipid medications, and biguanides vs thiazolidinedione were also readily initiated in these patients. This set the stage for various guidelines in the form of risk factor targets for disease. Albeit, these are moving targets at present, and we have yet to determine the optimal levels of systolic blood pressure and Hgb A1c targets for those with DM.<sup>63</sup> The investigators of the STENO trial concluded that only 5 patients would need to be treated intensively for an 8-year period to prevent 1 major CV event.

In the **Look Action for Health in Diabetes** (Look AHEAD) trial, patients who underwent intensive behavioural intervention had a significant reduction in weight (8.6% mean weight loss), Hgb A1c (mean 6.6% to 7.3%), waist circumference, and several other CV risk factors including blood pressure compared with overweight and obese diabetic participants who underwent DM-related education alone.<sup>64</sup> The study was halted after a 9.6-year follow-up because there was no significant difference in the primary CV outcome. The major reductions in many of the CV risk factors that were previously seen early in the trial had diminished differences over the nearly 10-year follow-up period, underscoring the difficulty in maintaining these interventions for a lifetime.<sup>65</sup>

There are certain interventions that can help reduce CV mortality in the setting of DM. Treating the “ABCs” (Hgb A1C%, blood pressure, LDL-C) individually has been shown to reduce the rates of complications associated with DM, in particular CVD.<sup>66-68</sup> Importantly, research on comprehensive risk reduction shows additional effects when meeting goals with multiple risk factors.<sup>66</sup> A study from Wong et al. combined data from the **Atherosclerosis Risk in Communities** (ARIC) study, the **Multi-Ethnic Study of Atherosclerosis** (MESA), and **Jackson Heart Study** (JHS) to examine CHD and CVD events in patients with DM.<sup>69</sup> Individuals with 1, 2, or all 3 risk factors at target levels had increasingly lower adjusted risks of CVD events of 36%, 52%, and 62%, respectively.

Another important aspect that the study was able to evaluate was the risk reduction associated with control of these factors. Those at blood pressure goal had a 17% reduction for CVD events and CHD, whereas those at LDL-C goal had a 33% and 41% reduction, respectively. Similarly, those at Hgb A1c goal targets had a 37% and 36% reduction in CVD events and CHD.<sup>69</sup> The overall conclusion was that patients would ultimately benefit from achieving all 3 goals.

Several studies have compared revascularization for stable CAD vs intensive healthy behavioural intervention and optimal medical therapy including more aggressive blood pressure, lipid, and Hgb A1c goals as a means to reduce CV risk in patients with DM. The **Bypass Angioplasty Revascularization Investigation 2 Diabetes** (BARI-2D) trial showed that revascularization in diabetic individuals with stable ischemic heart disease neither improved mortality nor decreased the rate of major CV events compared with optimal medical

therapy.<sup>70</sup> Hence, intensive behavioural modification is essential for improvement of CVD risk factors and reduction in mortality.<sup>71</sup> Comprehensive, multidisciplinary exercise-based cardiac rehabilitation (CR) programs are well validated care delivery models for optimal risk reduction.

## CR for the MetS and DM

Comprehensive, multidisciplinary exercise-based CR for secondary prevention of CVD, inclusive of an individualized and tailored approach to patient care is an effective means of improving long-term outcomes.<sup>72</sup> The provision of CR involves medical evaluation, prescribed exercise, risk factor modification, health education, and counselling.<sup>73</sup> The services are delivered over 4 phases including phase I (inpatient), phase II (the transition to outpatient supervision of a tailored exercise prescription), and phases III and IV (maintenance phases stressing long-term behavioural pattern changes).<sup>56</sup> As discussed by Sandesara et al.<sup>56</sup> in ACCSAP 9 learning module published by the American College of Cardiology, the benefits of CR in patients with CVD include a reduction in total and CVD mortality by 14% and 26%, respectively. CR can reduce rates of hospitalization, angina, and depression within this population and improve overall quality of life.<sup>56</sup> Furthermore, improvement in the maximum oxygen consumption and brachial artery flow-mediated dilation has been noted with high-intensity interval training, with a lower mean resting heart rate and body weight seen with moderate-intensity continuous training.<sup>74–76</sup>

## The MetS

The prevalence of MetS in the Canadian population was 21% among 18- to 79-year-old individuals, according to the 2013 results of the Canadian Health Measures Survey (CHMS). The prevalence of MetS in the Canadian population appears to increase with age, with the condition in 13% of 18- to 39-year-old individuals and 39% of those aged 60-79 years.<sup>77</sup> The exercise capacity of those with MetS who participate in CR has been noted to be significantly lower than individuals without MetS, and outcomes of CR are poorer in those with MetS.<sup>78</sup>

Individuals with MetS benefit from efforts to increase enrollment in CR programs. A meta-analysis of 15 studies with 19,325 subjects reported that CR decreased the prevalence of MetS by 25%. There was also a protective role on all components of MetS, including waist circumference (–2.25 cm), LDL-C (–11.93 mg/dL), HDL-C (+2.13 mg/dL), fasting glucose (–6.42 mg/dL), and systolic (–6.2 mm Hg) and diastolic (–2.53 mm Hg) blood pressure.<sup>73</sup> These benefits correlate with participation in CR, noting a linear relationship between the cumulative number of CR sessions attended, and outcomes (6% lower risk of MI with every 6 CR sessions attended).<sup>79</sup>

CV risk factors are also improved by CR participation. Small but significant reductions in obesity indices such as weight and BMI have been shown, along with significant improvements in peak exercise capacity, HDL-C and CRP levels, and quality of life.<sup>80</sup>



## DM

Healthy behaviour modification remain the most important approach to preventing DM, reducing risk almost twice as much as metformin alone.<sup>81,82</sup> In patients with DM, completion of CR is associated with a 54% reduction in mortality, 14% reduction in hospitalization, and 33% reduction in cardiac hospitalization.<sup>83</sup> There are data to support short-term, high-intensity (so-called “burst”) exercise over more traditional low-intensity, sustained exercise.<sup>84</sup> One study showed that in addition to greater improvement in their lipid profiles and BMI, patients who engaged in burst exercise experienced a 2.3-fold greater improvement in their Hgb A1c level ( $P < 0.01$ ) than those who participated in sustained exercise.<sup>84</sup>

Despite benefits of CR, patients with DM are less likely to complete the full course of CR compared to nondiabetic individuals (41% vs 56%;  $P < 0.0001$ ).<sup>83</sup> A meta-analysis published in the *Canadian Journal of Cardiology* revealed a sex difference of 4% (68.6% to 64.2% for men and women, respectively) in adherence to CR programs longer than 12 weeks' duration because of significant barriers that limit optimal participation and completion of CR.<sup>85</sup>

### Barriers to CR and Underutilization of Comprehensive CV Risk Reduction

Despite the well validated benefits of this approach to care, CR remains greatly underutilized. Of all eligible post-MI patients, less than 30% complete a prescribed program.<sup>86,87</sup> Factors affecting this include a lack of provider encouragement and patient participation once referred. Only 20% of patients eligible for CR are referred with major opportunities related to health system inadequacies.<sup>56,88</sup> Hospitals equipped with automated referral systems, such as the AHA's “Get with the Guidelines,” show far higher referral rates than the national average.<sup>86</sup> In addition, referrals in the general outpatient setting are on average 2 times lower than in cardiology or cardiac surgery clinics.<sup>88</sup> This is in part because of lack of familiarity with CR sites, limited access to proper referral forms, and logistical inconvenience for patients and providers.

The sociodemographic disparity apparent in the referral and utilization of CR is notable. Populations that have the lowest participation included women, uninsured patients, patients of low socioeconomic status, and elderly patients. A cross-sectional study also showed a low participation rate among rural patients.<sup>89</sup> There are many factors that promote this disparity. Cost is a prohibitive element for patients of low socioeconomic status or without adequate health insurance.<sup>56,89</sup> Similarly, distance travelled and transportation access to a CR site negatively affect participation rates in rural populations and for those of low socioeconomic status.<sup>89</sup> Despite the well-validated benefits of this approach to care, CR remains greatly underutilized. It is estimated that only about 30% of eligible post-MI patients complete a prescribed program. In one prospective study, 29% and 46% of patients participated in CR at 1 month and 6 months, respectively, from time of referral.<sup>90</sup> The proportion of patients referred to CR was observed to vary by 40% in a Canadian medical centre, according to the inpatient unit from which the patient was referred.<sup>91</sup> Importantly, the current model of CR delivery needs significant modification to overcome these barriers.

## The Rebranding of CR

The current model of CR delivery has numerous barriers, and efforts to improve program access and utilization are needed. Innovative CR delivery models incorporating use of telemedicine, internet-based, home-based, and community-based programs need to be implemented to improve utilization of CR.<sup>56,92</sup> With increasing population access to the Internet and mobile phones, telemedicine programs are promising alternatives to conventional centre-based programs with the potential for improved accessibility and reduced costs.<sup>56</sup> A meta-analysis of 11 trials showed that CR delivered via telehealth was equally effective as centre-based CR for improving modifiable CV risk factors and adherence.<sup>93</sup> Furthermore, home-based programs delivered by qualified nonphysician health professionals have similar outcomes in terms of mortality and CV risk factor modification compared with traditional centre-based programs.<sup>94</sup>

Mobile health or “M-health,” which takes advantage of mobile and wireless capabilities is emerging as a great tool for providers to connect with and track individuals’ health status reliably and remotely. M-health is an emerging approach to care built upon the telemedicine movement which has yet to establish any conclusive evidence of outcomes improvement.<sup>95–99</sup>

These alternative delivery models should not replace conventional CR programs but instead should be used to help overcome barriers.<sup>86</sup>

## Conclusions

The epidemic of MetS and DM continues to grow along with resultant consequences and complications. Comprehensive CV risk reduction is critical for this high-risk population. Health behaviour management with a focus on physical activity and diet is central to reducing ASCVD risk. Population health initiatives such as the AHA 2020, Canadian Diabetes Strategy, and World Heart Federation/WHO 25by25 are important for health promotion and disease prevention. Comprehensive, multidisciplinary exercise-based CR has well validated efficacy in reducing mortality in patients with CVD. CR is associated with a reduction in prevalence of MetS and provides a protective role in reducing negative risk factors associated with MetS. In diabetic individuals, CR participation is associated with reduced mortality and hospitalization in addition to improvements in lipid levels, BMI, fitness, and Hgb A1c levels. Despite these benefits, CR referral, enrollment, participation, and completion continue to be suboptimal because of barriers that confront patients and providers. Incorporating new care models and modes of CR delivery have the potential to enhance the benefits of comprehensive CV risk reduction and CR utilization.

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## References

1. World Health Organization. [April 20, 2016] The Top 10 Causes of Death. Available at: <http://www.who.int/mediacentre/factsheets/fs310/en/index4.html>.
2. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*. 2004; 109:433–8. [PubMed: 14744958]
3. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009; 120:1640–5. [PubMed: 19805654]
4. Medscape. [April 17, 2016] NCEP Definition of Metabolic Syndrome Better Predictor Than IDF of Diabetes in Women. Available at: <http://www.medscape.com/viewarticle/580395>.
5. Fuller JH, Stevens LK, Wang SL. Risk factors for cardiovascular mortality and morbidity: the WHO Multinational Study of Vascular Disease in Diabetes. *Diabetologia*. 2001; 44(suppl 2):S54–64. [PubMed: 11587051]
6. Beland Y. Canadian community health survey methodological overview. *Health Rep*. 2002; 13:9–14.
7. Statistics Canada. Body Mass Index, Overweight or Obese, Self-Reported, Adult, by Age Group and Sex (Table). Statistics Canada, Government of Canada; 2014.
8. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics 2014 update: a report from the American Heart Association. *Circulation*. 2014; 129:e28–292. [PubMed: 24352519]
9. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. Adults. *Diabetes Care*. 2004; 27:2444–9. [PubMed: 15451914]
10. Fall CH. Non-industrialised countries and affluence. *Br Med Bull*. 2001; 60:33–50. [PubMed: 11809617]
11. Beltran-Sanchez H, Harhay MO, Harhay MM, McElligott S. Prevalence and trends of metabolic syndrome in the adult U.S. population, 1999–2010. *J Am Coll Cardiol*. 2013; 62:697–703. [PubMed: 23810877]
12. Finkelstein MM. The prevalence of diabetes among overweight and obese individuals is higher in poorer than in richer neighbourhoods. *Can J Diabetes*. 2008; 32:190–7.
13. Riediger ND, Clara I. Prevalence of metabolic syndrome in the Canadian adult population. *CMAJ*. 2011; 183:E1127–34. [PubMed: 21911558]
14. International Diabetes Federation. *Diabetes Atlas*. 2nd Ed.. International Diabetes Federation; Brussels, Belgium: 2003.
15. *Diabetes in Canada: Facts and Figures From a Public Health Perspective*. Public Health Agency of Canada; Ottawa, Ontario: 2011.
16. Association TCD. , editor. *The Diabetes Charter for Canada*. diabetesca/charter; 2015.
17. Willett WC, Dietz WH, Colditz GA. Guidelines for healthy weight. *N Engl J Med*. 1999; 341:427–34. [PubMed: 10432328]
18. Neeland IJ, Ayers CR, Rohatgi AK, et al. Associations of visceral and abdominal subcutaneous adipose tissue with markers of cardiac and metabolic risk in obese adults. *Obesity (Silver Spring)*. 2013; 21:E439–47. [PubMed: 23687099]
19. Tchernof A, Despres JP. Pathophysiology of human visceral obesity: an update. *Physiol Rev*. 2013; 93:359–404. [PubMed: 23303913]
20. Medina-Gomez G, Virtue S, Lelliott C, et al. The link between nutritional status and insulin sensitivity is dependent on the adipocyte-specific peroxisome proliferator-activated receptor-gamma2 isoform. *Diabetes*. 2005; 54:1706–16. [PubMed: 15919792]
21. Lyon CJ, Law RE, Hsueh WA. Minireview: adiposity, inflammation, and atherogenesis. *Endocrinology*. 2003; 144:2195–200. [PubMed: 12746274]
22. Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr*. 2004; 92:347–55. [PubMed: 15469638]

23. Rosenson RS. Assessing risk across the spectrum of patients with the metabolic syndrome. *Am J Cardiol.* 2005; 96:8e–10e.
24. Juhan-Vague I, Alessi MC, Vague P. Increased plasma plasminogen activator inhibitor 1 levels. A possible link between insulin resistance and atherothrombosis. *Diabetologia.* 1991; 34:457–62. [PubMed: 1916049]
25. Sattar N, Gaw A, Scherbakova O, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation.* 2003; 108:414–9. [PubMed: 12860911]
26. Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA.* 2002; 288:2709–16. [PubMed: 12460094]
27. Malik S, Wong ND, Franklin SS, et al. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. *Circulation.* 2004; 110:1245–50. [PubMed: 15326067]
28. Wang J, Ruotsalainen S, Moilanen L, et al. The metabolic syndrome predicts cardiovascular mortality: a 13-year follow-up study in elderly non-diabetic Finns. *Eur Heart J.* 2007; 28:857–64. [PubMed: 17303589]
29. Wang J, Ruotsalainen S, Moilanen L, et al. The metabolic syndrome predicts incident stroke: a 14-year follow-up study in elderly people in Finland. *Stroke.* 2008; 39:1078–83. [PubMed: 18323501]
30. Cubbon RM, Wheatcroft SB, Grant PJ, et al. Temporal trends in mortality of patients with diabetes mellitus suffering acute myocardial infarction: a comparison of over 3000 patients between 1995 and 2003. *Eur Heart J.* 2007; 28:540–5. [PubMed: 17289742]
31. Aronson D. Hyperglycemia and the pathobiology of diabetic complications. *Adv Cardiol.* 2008; 45:1–16. [PubMed: 18230953]
32. Morrish NJ, Wang SL, Stevens LK, Fuller JH, Keen H. Mortality and causes of death in the WHO Multinational Study of Vascular Disease in Diabetes. *Diabetologia.* 2001; 44(suppl 2):S14–21. [PubMed: 11587045]
33. Prevention CfDca. National Diabetes Statistics Report: Estimates of Diabetes and its Burden in the United States. The Centers for Disease Control and Prevention; Atlanta, GA: 2014.
34. Lloyd-Jones DM, Leip EP, Larson MG, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation.* 2006; 113:791–8. [PubMed: 16461820]
35. Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med.* 2008; 358:580–91. [PubMed: 18256393]
36. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. *Diabetes Care.* 2005; 54:1615–25.
37. Go AS, Mozaffarian D, Roger VL, et al. Executive summary: heart disease and stroke statisticse2013 update: a report from the American Heart Association. *Circulation.* 2013; 127:143–52. [PubMed: 23283859]
38. Sperling LS, Mechanick JI, Neeland IJ, et al. The CardioMetabolic Health Alliance: working toward a new care model for the metabolic syndrome. *J Am Coll Cardiol.* 2015; 66:1050–67. [PubMed: 26314534]
39. Centers for Disease Control and Prevention. State Indicator Report on Physical Activity, 2010. US Department of Health and Human Services; Atlanta, GA: 2010.
40. Rutkow L, Vernick JS, Hodge JG, Teret SP. Preemption and the obesity epidemic: state and local menu labeling laws and the nutrition labeling and education act. *J Law Med Ethics.* 2008; 36:772–89. [PubMed: 19094006]
41. Okie S. New York to trans fats: you're out! *N Engl J Med.* 2007; 356:2017–21. [PubMed: 17507699]
42. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014; 63:2960–84. [PubMed: 24239922]
43. Soltani S, Shirani F, Chitsazi MJ, Salehi-Abargouei A. The effect of Dietary Approaches to Stop Hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. *Obes Rev.* 2016; 17:442–54. [PubMed: 26990451]

44. Estruch R, Martinez-Gonzalez MA, Corella D, et al. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med.* 2006; 145:1–11. [PubMed: 16818923]
45. Freedland SJ, Aronson WJ, Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, Golan R, Fraser D, Bolotin A, Vardi H, Tangi-Rozental O, Zuk-Ramot R, Sarusi B, Brickner D, Schwartz Z, Sheiner E, Marko R, Katorza E, Thiery J, Fiedler GM, Blucher M, Stumvoll M, Stampfer MJ, Dietary Intervention Randomized Controlled Trial (DIRECT) Group. Words of wisdom. Re: weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med.* 2008; 359:229e41. [PubMed: 18635428] *Eur Urol.* 2009; 55:249–50. [PubMed: 20050018]
46. Esposito K, Maiorino MI, Ciotola M, et al. Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial. *Ann Intern Med.* 2009; 151:306–14. [PubMed: 19721018]
47. Elhayany A, Lustman A, Abel R, Attal-Singer J, Vinker S. A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study. *Diabetes Obes Metab.* 2010; 12:204–9. [PubMed: 20151996]
48. Shen J, Wilmot KA, Ghasemzadeh N, et al. Mediterranean dietary patterns and cardiovascular health. *Annu Rev Nutr.* 2015; 35:425–49. [PubMed: 25974696]
49. Kastorini CM, Milionis HJ, Esposito K, et al. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. *J Am Coll Cardiol.* 2011; 57:1299–313. [PubMed: 21392646]
50. Estruch R, Ros E, Salas-Salvado J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med.* 2013; 368:1279–90. [PubMed: 23432189]
51. Huo R, Du T, Xu Y, et al. Effects of Mediterranean-style diet on glycemic control, weight loss and cardiovascular risk factors among type 2 diabetes individuals: a meta-analysis. *Eur J Clin Nutr.* 2015; 69:1200–8. [PubMed: 25369829]
52. Babio N, Bullo M, Salas-Salvado J. Mediterranean diet and metabolic syndrome: the evidence. *Public Health Nutr.* 2009; 12:1607–17. [PubMed: 19689829]
53. Salas-Salvado J, Guasch-Ferre M, Lee CH, et al. Protective effects of the Mediterranean diet on type 2 diabetes and metabolic syndrome. *J Nutr.* 2016; 146:930S–7S.
54. de Lorgeril M, Salen P, Martin JL, et al. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation.* 1999; 99:779–85. [PubMed: 9989963]
55. Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA.* 2004; 292:1440–6. [PubMed: 15383514]
56. Sandesara PB, Lambert CT, Gordon NF, et al. Cardiac rehabilitation and risk reduction: time to “rebrand and reinvent.”. *J Am Coll Cardiol.* 2015; 65:389–95. [PubMed: 25634839]
57. Physical Activity Guidelines Advisory Committee report, 2008. To the Secretary of Health and Human Services. Part A: executive summary. *Nutr Rev.* 2009; 67:114–20. [PubMed: 19178654]
58. Johnson JL, Slentz CA, Houmard JA, et al. Exercise training amount and intensity effects on metabolic syndrome (from Studies of a Targeted Risk Reduction Intervention through Defined Exercise). *Am J Cardiol.* 2007; 100:1759–66. [PubMed: 18082522]
59. Slentz CA, Aiken LB, Houmard JA, et al. Inactivity, exercise, and visceral fat. STRRIDE: a randomized, controlled study of exercise intensity and amount. *J Appl Physiol (1985).* 2005; 99:1613–8. [PubMed: 16002776]
60. AbouAssi H, Slentz CA, Mikus CR, et al. The effects of aerobic, resistance, and combination training on insulin sensitivity and secretion in overweight adults from STRRIDE AT/RT: a randomized trial. *J Appl Physiol (1985).* 2015; 118:1474–82. [PubMed: 25882384]
61. Wong ND, Patao C, Wong K, et al. Trends in control of cardiovascular risk factors among US adults with type 2 diabetes from 1999 to 2010: comparison by prevalent cardiovascular disease status. *Diabetes Vasc Dis Res.* 2013; 10:505–13.
62. Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med.* 2003; 348:383–93. [PubMed: 12556541]

63. Franz MJ, Boucher JL, Evert AB. Evidence-based diabetes nutrition therapy recommendations are effective: the key is individualization. *Diabetes Metab Syndr Obes.* 2014; 7:65–72. [PubMed: 24591844]
64. Wing RR, Lang W, Wadden TA, et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care.* 2011; 34:1481–6. [PubMed: 21593294]
65. Look AHEAD Research Group. Wing RR, Bolin P, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes [erratum in 2014;370:1866]. *N Engl J Med.* 2013; 369:145–54. [PubMed: 23796131]
66. *Lancet.* Vol. 352. UK Prospective Diabetes Study (UKPDS) Group; 1998. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33); p. 837-53.erratum in 1999;354:602
67. Hansson, L., Zanchetti, A., Carruthers, SG., et al. *Lancet.* Vol. 351. HOT Study Group; 1998. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial.; p. 1755-62.
68. Grover SA, Coupal L, Zowall H, Dorais M. Cost-effectiveness of treating hyperlipidemia in the presence of diabetes : who should be treated? *Circulation.* 2000; 102:722–7. [PubMed: 10942738]
69. Wong MG, Perkovic V, Chalmers J, et al. Long-term benefits of intensive glucose control for preventing end-stage kidney disease: ADVANCE-ON. *Diabetes Care.* 2016; 39:694–700. [PubMed: 27006512]
70. BARI 2D Study Group. Frye RL, August P, et al. A randomized trial of therapies for type 2 diabetes and coronary artery disease. *N Engl J Med.* 2009; 360:2503–15. [PubMed: 19502645]
71. Acharjee S, Teo KK, Jacobs AK, et al. Optimal medical therapy with or without percutaneous coronary intervention in women with stable coronary disease: a pre-specified subset analysis of the Clinical Outcomes Utilizing Revascularization and Aggressive druG Evaluation (COURAGE) trial. *Am Heart J.* 2016; 173:108–17. [PubMed: 26920603]
72. Varghese T, Schultz WM, McCue AA, et al. Physical activity in the prevention of coronary heart disease: implications for the clinician. *Heart.* 2016; 102:904–9. [PubMed: 26941396]
73. Sadeghi M, Salehi-Abargouei A, Kasaei Z, et al. Effect of cardiac rehabilitation on metabolic syndrome and its components: a systematic review and meta-analysis. *J Res Med Sci.* 2016;21. [PubMed: 27904567]
74. Liou K, Ho S, Fildes J, Ooi SY. High intensity interval versus moderate intensity continuous training in patients with coronary artery disease: a meta-analysis of physiological and clinical parameters. *Heart Lung Circ.* 2016; 25:166–74. [PubMed: 26375499]
75. Ramos JS, Dalleck LC, Tjonna AE, Beetham KS, Coombes JS. The impact of high-intensity interval training versus moderate-intensity continuous training on vascular function: a systematic review and meta-analysis. *Sports Med.* 2015; 45:679–92. [PubMed: 25771785]
76. Elliott AD, Rajopadhyaya K, Bentley DJ, Beltrame JF, Aromataris EC. Interval training versus continuous exercise in patients with coronary artery disease: a meta-analysis. *Heart Lung Circ.* 2015; 24:149–57. [PubMed: 25306500]
77. Metabolic syndrome in adults, 2012 to 2013. Statistics Canada; 2015. Available at: <http://www.statcan.gc.ca/pub/82-625-x/2014001/article/14123-eng.htm> [April 20, 2016]
78. Myers J, Prakash M, Froelicher V, et al. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med.* 2002; 346:793–801. [PubMed: 11893790]
79. Hammill BG, Curtis LH, Schulman KA, Whellan DJ. Relationship between cardiac rehabilitation and long-term risks of death and myocardial infarction among elderly Medicare beneficiaries. *Circulation.* 2010; 121:63–70. [PubMed: 20026778]
80. Lavie CJ, Morshedi-Meibodi A, Milani RV. Impact of cardiac rehabilitation on coronary risk factors, inflammation, and the metabolic syndrome in obese coronary patients. *J Cardiometab Syndr.* 2008; 3:136–40. [PubMed: 18983328]
81. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* 2002; 346:394–403.

82. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001; 344:1343–50. [PubMed: 11333990]
83. Armstrong MJ, Sigal RJ, Arena R, et al. Cardiac rehabilitation completion is associated with reduced mortality in patients with diabetes and coronary artery disease. *Diabetologia*. 2015; 58:691–8. [PubMed: 25742772]
84. Pandey AK, Clarus S, Poirier P. The comparative effects of burst exercise versus sustained exercise on the cardiometabolic status of newly diagnosed diabetic patients. *Can J Cardiol*. 2015; 31:S207–8.
85. Oosenbrug, E., Marinho, RP., Zhang, J., et al. [April 20, 2016] Sex differences in cardiac rehabilitation adherence: a meta-analysis [e-pub ahead of print].. *Can J Cardiol*. <http://dx.doi.org/10.1016/j.cjca.2016.01.036>
86. Balady G. Referral, enrollment, and delivery of cardiac rehabilitation/ secondary prevention programs at clinical centers and beyond: a presidential advisory from the American Heart Association. *Circulation*. 2011; 124:2951–60. [PubMed: 22082676]
87. Thomas RJ, King M, Lui K, et al. ReprintAACVPR/ACCF/AHA 2010 update: performance measures on cardiac rehabilitation for referral to cardiac rehabilitation/secondary prevention services: a report of the American Association of Cardiovascular and Pulmonary Rehabilitation and the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures (Writing Committee to Develop Clinical Performance Measures for Cardiac Rehabilitation) [erratum in 2010;90:1906]. *Phys Ther*. 2010; 90:1373–82.
88. Menezes AR, Lavie CJ, Milani RV, et al. Cardiac rehabilitation in the United States. *Prog Cardiovasc Dis*. 2014; 56:522–9. [PubMed: 24607017]
89. Shanmugasagaram S, Oh P, Reid RD, McCumber T, Grace SL. Cardiac rehabilitation barriers by rurality and socioeconomic status: a cross-sectional study. *Int J Equity Health*. 2013; 12:72. [PubMed: 23985017]
90. Parashar S, Spertus JA, Tang F, et al. Predictors of early and late enrollment in cardiac rehabilitation, among those referred, after acute myocardial infarction. *Circulation*. 2012; 126:1587–95. [PubMed: 22929302]
91. Ali-Faisal SF, Benz Scott L, Johnston L, Grace SL. Cardiac rehabilitation referral and enrolment across an academic health sciences centre with eReferral and peer navigation: a randomised controlled pilot trial. *BMJ Open*. 2016; 6:e010214.
92. Lavie CJ, Arena R, Franklin BA. Cardiac rehabilitation and healthy lifestyle interventions: rectifying program deficiencies to improve patient outcomes. *J Am Coll Cardiol*. 2016; 67:13–5. [PubMed: 26764060]
93. Rawstorn JC, Gant N, Direito A, Beckmann C, Maddison R. Telehealth exercise-based cardiac rehabilitation: a systematic review and meta-analysis. *Heart*. 2016; 102:1183–92. [PubMed: 26936337]
94. Taylor RS, Dalal H, Jolly K, Moxham T, Zawada A. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev*. 2010:CD007130. [PubMed: 20091618]
95. Flodgren G, Rachas A, Farmer AJ, Inzitari M, Shepperd S. Interactive telemedicine: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev*. 2015:Cd002098. [PubMed: 26343551]
96. Chow CK, Ariyaratna N, Islam SM, Thiagalingam A, Redfern J. mHealth in cardiovascular health care. *Heart Lung Circ*. 2016; 25:802–7. [PubMed: 27262389]
97. Bloss CS, Wineinger NE, Peters M, et al. A prospective randomized trial examining health care utilization in individuals using multiple smartphone-enabled biosensors. *PeerJ*. 2016; 4:e1554. [PubMed: 26788432]
98. Omboni, S., Caserini, M., Coronetti, C. [April 20, 2016] Telemedicine and m-health in hypertension management: technologies, applications and clinical evidence [e-pub ahead of print].. *High Blood Press Cardiovasc Prev*. <http://dx.doi.org/10.1007/s40292-016-0143-6>
99. Cajita MI, Gleason KT, Han HR. A systematic review of mhealth-based heart failure interventions. *J Cardiovasc Nurs*. 2016; 31:E10–22.

**Table 1**

AHA/NHLBI criteria for the clinical diagnosis of metabolic syndrome (any 3 of the following 5)

Measure	Categorical cut point
Elevated waist circumference *	102 cm ( 40 inches) in men; 88 cm ( 35 inches) in women
Elevated triglycerides	150 mg/dL (1.7 mmol/L)
Reduced HDL-C	< 40 mg/dL (1.03 mmol/L) in men; < 50 mg/dL (1.3 mmol/L) in women; Or receiving drug treatment for reduced HDL-C
Elevated blood pressure	130 mm Hg systolic blood pressure; 85 mm Hg diastolic blood pressure; Or receiving antihypertensive medication in a patient with a history of hypertension
Elevated fasting glucose	100 mg/dL; Or receiving drug treatment for elevated glucose level

AHA, American Heart Association; HDL-C, high-density lipoprotein cholesterol; NHLBI, National Heart, Lung, and Blood Institute.

Modified from Grundy et al.<sup>2</sup> with permission from Wolters Kluwer Health, Inc.

\* ATP III clinical identification of the metabolic syndrome.



**Table 2**

IDF recommended waist circumference thresholds for abdominal obesity

	<b>Men</b>	<b>Women</b>
Europid	94 cm (37.0 inches)	80 cm (31.5 inches)
South Asian	90 cm (35.4 inches)	80 cm (31.5 inches)
Chinese	90 cm (35.4 inches)	80 cm (31.5 inches)
Japanese	85 (33.5 inches)	90 cm (35.4 inches)

IDF, International Diabetes Foundation.

Modified from Alberti et al.<sup>3</sup> with permission from Wolters Kluwer Health, Inc.

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