

# Assessing and Managing Risk for Cardiovascular Disease: A Worldwide Perspective

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## Abstract

**Cardiovascular disease (CVD) has become increasingly recognized as a major cause of disability, premature death, and escalating health-care costs throughout the world. The purpose of the present report is to review the most widely used worldwide tools for assessment of the total (absolute, global, integrated) risk of developing CVD during the next 5 or 10 years and to review guidelines for the clinical management of dyslipidemia, hypertension, and dysglycemia that incorporate these tools. The World Health Organization (WHO) / International Society of Hypertension (ISH) risk charts, The Framingham system, Systematic Coronary Risk Evaluation (SCORE) charts, and the PROCAM (PROspective Cardiovascular Munster) Quick Check and Health Check systems are described. Since the use of clinical guidelines based on these tools has some limitations and challenges, alternative or modified approaches for the management of CVD risk factors have been proposed by several researchers recently. Future studies are needed to evaluate the effectiveness of these proposed strategies.**

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**Key Words:** *cardiovascular disease risk factors, global risk, risk charts, assessment, management*

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## Introduction

For many years, infectious diseases, especially during the perinatal and early childhood period, have been the leading causes of mortality in middle- or low-income settings.<sup>1</sup> Over the past few decades, urbanization, aging, and globalized lifestyle changes have increased the relative importance of

chronic disease in countries with low or intermediate levels of income.<sup>2</sup> Unfortunately, reporting on causes of death across the world has been hindered by limited, incomplete, and uncertain data, but some estimates are available.<sup>3</sup> According to the 2004 estimates by World Health Organization (WHO), heart diseases and stroke are the leading causes of all deaths worldwide, with more than 80% of these deaths occurring in low- or middle-income countries.<sup>3</sup> Thus, cardiovascular disease (CVD) has become increasingly recognized as a major cause of disability, premature death, and escalating health-care costs throughout the world.<sup>4</sup>

The development of CVD is an extraordinarily complex process that results from the interplay of biological, socioeconomic, and environmental factors.<sup>5</sup> Two major preventive strategies, namely a population-based approach to promote the overall health status of the community and a clinical medicine approach aimed at high-risk individuals (who require more aggressive modification of risk factors) are in use for addressing the burden of CVD (**Figure 1**).<sup>6-8</sup>

The effectiveness of population-based interventions has been demonstrated in several countries; for example, national interventions to reduce intake of saturated fat (in Great Britain, Finland, and the US), intake of sodium (Finland and Japan), and smoking (Great Britain, Finland, the US, and Japan) led to a precipitous decline in mortality from heart disease and stroke in those countries.<sup>9-12</sup> Indeed, the majority of cases of CVD occur in individuals with low risk simply because they represent a large proportion of the population.<sup>13</sup> Moreover, according to recent estimates based on data pooled from six European cohorts of the general population, a 10-year reduction of 10% in the prevalence of each of three major CVD risk factors (high blood cholesterol, high blood pressure, and smoking) could save 9,125 lives per 1 million persons in the population.<sup>13</sup> In contrast, a hypothetical “complete compliance” treatment of all high-risk individuals with a polypill containing statins, antihypertensives, and aspirin would save 1,861-7,452 lives per million.<sup>13</sup> In addition, the successful implementation of population-level interventions not only may be effective in decreasing CVD mortality but may also contribute to decreasing the number of persons requiring medications and follow-up visits.

To address the management of CVD risk factors (including

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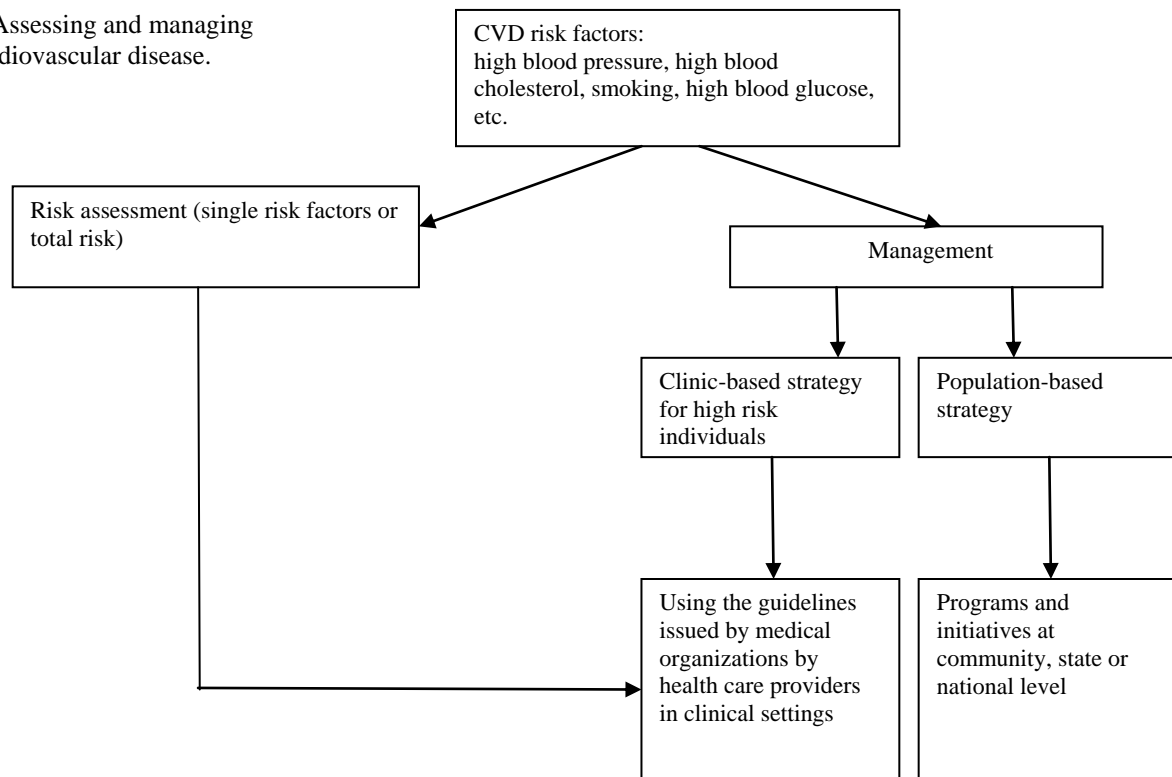
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dyslipidemia, hypertension, and dysglycemia) at the individual level in clinical settings various practice guidelines for the screening, diagnosis, and treatment have been developed by major medical organizations.<sup>14</sup> However, it has been recognized that in an individual person, risk factors rarely occur in isolation, and summary indexes based on several risk factors are better predictors of subsequent CVD event than are single risk factors.<sup>15</sup> The total (absolute, “global”, integrated) CVD risk, a probability indicator of developing CVD during the next 5 or 10 years that accounts

for several major CVD risk factors, can be derived from longitudinal studies. Thus, many current clinical practice guidelines now incorporate the estimation of a patient's total CVD risk.<sup>5</sup> This risk can be estimated by combining risk factors in a fast growing number of readily accessible tools that include models, point systems, or charts.<sup>5</sup> The clinical guidelines for the management of CVD risk factors including the tools estimating total CVD risk and the management of CVD risk factors including the tools estimating total CVD risk and the treatment target goals

**Figure 1.** Assessing and managing risk for cardiovascular disease.



for single risk factors (levels of blood pressure, blood lipids, and blood glucose) vary widely by region or country.

The purpose of the present report is to review the most widely used worldwide tools for assessment of the total (absolute, global, integrated) risk of developing CVD during the next 5 or 10 years and to review guidelines for the clinical management of dyslipidemia, hypertension, and dysglycemia that incorporate these tools. Publications were identified by performing 3 different computerized searches of the PubMed database. The first search included terms such as “global, regional, chronic disease, death”. The second search consisted of terms “cardiovascular risk assessment”, “cardiovascular risk management”, “Framingham”, “World Health Organization (WHO) risk charts”, “Systematic Coronary Risk Evaluation (SCORE)”, and “the PROCAM (PROspective Cardiovascular Munster)”. The third search focused on the following terms “cholesterol prevalence treatment control”, “dyslipidemia prevalence treatment control”, “hypertension prevalence treatment control” and “the US”, “Great Britain”, “United Kingdom”, “Finland”,

“Japan”, “Europe”, “Asia”, “China”, “developing countries”, “middle- and low-income countries”, “Japan”, “the Asia-Pacific Cohort Studies Collaboration study”, and “World Health Organization (WHO)”. The papers published from the 2005-April 2010 and from the 1995-April 2010 were evaluated during the first or last searches and the second search, respectively. Other sources included reference books and selected websites identified by using “Google” search engine. Studies, books, and websites were considered for inclusion if they were written in English language, had relevant applications to the assessment of global cardiovascular risk profile, and were published in “the PubMed core clinical journals”.

### **Systems for Assessing the Risk of CVD and Clinical Guidelines Incorporating Them**

*World Health Organization (WHO) / International Society of Hypertension (ISH)*

The WHO / International Society of Hypertension (ISH) risk charts can be used to predict the 10-year absolute risk of stroke and heart attack in adults aged 40-79 years by using

just six risk factors: sex, age, systolic blood pressure, smoking status, diabetes, and total blood cholesterol concentrations.<sup>4</sup> The color-coded, easy-to-use charts were developed for 14 WHO subregions. Charts allowing risk estimation without measuring blood cholesterol, which are particularly suitable for low resource settings, are also available. These risk charts have been recommended for use by the WHO/ISH Guidelines for Assessment and Management of Cardiovascular Risk.<sup>4</sup> An estimate of the patient's risk or the actual presence of established heart disease, stroke, peripheral vascular disease, or diabetes, is used to guide the physician in making decisions for nicotine replacement, antihypertensive, lipid-lowering, or antiplatelet therapy. The recommended frequency of follow-up visits and treatment by five different risk categories is shown in **Table 1**. The major limitation of these guidelines is that they were developed by creating a hypothetical dataset for each subregion but were not validated. The charts for estimating risk can be found at

[http://www.who.int/cardiovascular\\_diseases/guidelines/PocketGL.ENGLISH.AFR-D-E.rev1.pdf](http://www.who.int/cardiovascular_diseases/guidelines/PocketGL.ENGLISH.AFR-D-E.rev1.pdf)

### **Framingham**

The Framingham system for predicting risk of CHD is derived from the Framingham Heart Study (Framingham, Massachusetts, USA) and is probably the most widely used globally.<sup>16</sup> This method estimates the risk of two clinical CVD endpoints over the course of 10 years, myocardial infarction and coronary death, among adults aged 30-75 years who do not currently have heart disease or diabetes; other heart and vascular diseases are not included. The latest Framingham risk system was revised to calculate the 10-year risk of all first CVD events, including CHD, cerebrovascular disease, peripheral vascular disease, and heart failure.<sup>16</sup> The factors used to calculate risk of CHD (as a percentage) include age, sex, systolic blood pressure, smoking status, and two cholesterol measurements (total cholesterol and high-density lipoprotein cholesterol (HDL-C)). Finally, to complement the currently available 10-year risk algorithm, an equation for prediction of 30-year risk of CVD endpoints including coronary death, myocardial infarction, or stroke among 4,500 participants of the Framingham Offspring cohort was recently developed.<sup>17</sup>

Originally, the Framingham system was developed as a complex equation which was simplified later into a point-based system for clinical practice. A point system can be found at

[http://www.nhlbi.nih.gov/guidelines/cholesterol/risk\\_tbl.htm](http://www.nhlbi.nih.gov/guidelines/cholesterol/risk_tbl.htm). In addition, online calculators are available at <http://hp2010.nhlbihin.net/atp3iii/calculator.asp?usertype=prof>.

The estimated risk of CHD over the course of 10 years from the original Framingham equation or point-based system is used in the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines for management of lipid disorders<sup>18</sup> (**Table 2**) and in recommendation for using aspirin to prevent CVD in the United States.<sup>19,20</sup> In addition, The Framingham 1991 risk

equations are recommended by Great Britain's National Institute for Health and Clinical Excellence (NICE) guidelines on the management of blood lipid levels for the primary and secondary prevention of CVD.<sup>21</sup> Although the Framingham system is well calibrated to predict first coronary events in populations from the United States, Australia, and New Zealand, it may overestimate or underestimate risk in other populations.<sup>5</sup> Indeed, the original Framingham functions overestimated the risk of CHD among 30,000 participants from the Chinese Multi-Provincial Cohort Study (CMCS).<sup>22</sup> However, the results of this study demonstrated that recalibration of the Framingham functions using the mean values of risk factors and mean CHD incidence rates of the specific cohort may be used for improvement of CHD risk prediction algorithms. Since stroke is the predominant cardiovascular disease in China, the other studies using data from the Chinese cohorts integrated CHD and stroke, added body mass index in the risk prediction model, and/or derived the simplified point score system for prediction 10 year risk of CHD and stroke for the Chinese population.<sup>23,24</sup>

Recently, data from the Framingham Heart Study was also used to develop a scoring system for predicting the 1-, 2-, and 4-year risk for new-onset hypertension.<sup>25</sup> Age, sex, systolic and diastolic blood pressure, body mass index, parental hypertension, and cigarette smoking all emerged as significant risk factors for the onset of hypertension. The risk calculator, which is in Microsoft Excel, can be found online at <http://www.annals.org/content/148/2/102/suppl/DC1>.

Finally, the Framingham Hypertension Risk Score (described above) performed well in a European population as reported in the Whitehall II Study.<sup>26</sup>

### **Systematic Coronary Risk Evaluation (SCORE)**

The SCORE system is based on a large, pooled dataset of 12 European prospective studies.<sup>27</sup> In SCORE the risk is defined as the absolute 10-year probability of a fatal cardiovascular event (mortality from acute myocardial infarction, stroke, aortic aneurysm, or other). The charts, which include five parameters (sex, smoking status, systolic blood pressure, total cholesterol, and age) are color coded and easy to use. A chart of relative risk illustrating that young persons with a low absolute risk may still have a substantially higher relative risk than their peers and could benefit from the interventions available. Patients with established CVD and diabetes are placed in the high-risk group without a calculation of their risk, and a risk of CVD death of 5% or greater among the other participants is considered high risk. In Europe, guidelines developed by the Fourth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice incorporate the SCORE system. The guidelines take into account the multifactorial nature of CVD and allow flexibility in management (the major features of the guidelines are summarized in **Table 3**). The full text, executive summary, and pocket version of guidelines can be found online at: <http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/cvd-prevention.aspx>.

**Table 1.** Management of CVD risk factors based on the World Health Organization (WHO) / International Society of Hypertension (ISH) guidelines.

Step 1: Total CVD risk estimation using the WHO / ISH charts: [http://www.who.int/cardiovascular\\_diseases/guidelines/PocketGL.ENGLISH.AFR-D-E.rev1.pdf](http://www.who.int/cardiovascular_diseases/guidelines/PocketGL.ENGLISH.AFR-D-E.rev1.pdf); World Health Organization. Prevention of Cardiovascular Disease: Guidelines for assessment and management of cardiovascular risk. Pocket Guidelines for Assessment and Management of Cardiovascular Risk; Geneva, 2007, Accessed April 20, 2010.

Step 2: Clinical management:

Risk category (10-year risk of CVD: stroke and heart attack)	Re-assessment	Nicotine replacement therapy	Antihypertensive therapy <sup>a, b</sup>	Lipid-lowering therapy <sup>b</sup>	Antiplatelet therapy	Other targets and therapy
<b>Low: &lt;10%</b>	Every 2-5 years		Blood pressure at $\geq 160/100$ mmHg or target organ damage is present.	Total cholesterol at or above 8 mmol/L / 320 mg/dL.	Aspirin should <i>not</i> be given.	
<b>Moderate: 10% to &lt;20%</b>	Every 6-12 months		Blood pressure at $\geq 160/100$ mmHg or target organ damage is present.	Total cholesterol at or above 8 mmol/L / 320 mg/dL.	Aspirin should <i>not</i> be given.	
<b>High: 20% to &lt;30%</b>	Every 6-12 months	Nicotine replacement therapy and/or nortriptyline or amfebutamone (bupropion) should be offered to motivated smokers who fail to quit with counseling.	Persistent high blood pressure ( $\geq 140/80$ mmHg).	Persistently high total serum cholesterol ( $>5.0$ mmol/L / 190 mg/dL) and/or LDL cholesterol $>3.0$ mmol/L / 115 mg/dL.	Aspirin should probably <i>not</i> be given.	
<b>Very high: <math>\geq 30%</math></b>	Every 6-12 months		Persistent blood pressure $\geq 130/80$ mm/Hg.	Total serum cholesterol should be reduced to less than 5.0 mmol/L / 190 mg/dL (LDL cholesterol to below 3.0 mmol/L / 115 mg/dL) or by 25% (30% for LDL cholesterol), whichever is greater.	Individuals in this risk category should be given low-dose aspirin.	
<b>Established CVD or diabetes</b>	Every 6-12 months	Nicotine replacement therapy should be offered to individuals who continue to smoke at least 10 cigarettes a day or more.  Nonsmoking people should be advised to avoid exposure to secondhand tobacco smoke as much as possible.	Persistent high blood pressure ( $\geq 140/80$ mmHg)  If stroke or transient ischemic attack: persistent blood pressure $\geq 130/80$ mm/Hg.	Total serum cholesterol should be reduced to less than 4.0 mmol/L / 152 mg/dL (LDL cholesterol to below 2.0 mmol/L / 77 mg/dL) or by 25% (30% for LDL cholesterol), whichever is greater.	Individuals in this risk category should be given low-dose aspirin.	Persistent fasting blood glucose $>6$ mmol/L (metformin and/or insulin).  Myocardial infarction: beta-blockers and ACE inhibitors (long-term, probably lifelong).  Stroke or transient ischemic attack and atrial fibrillation: anticoagulation therapy.

(Table 1) **Abbreviations:** ACE: angiotensin-converting enzyme; LDL: low-density lipoprotein.

<sup>a</sup>Thiazide-like diuretic, ACE inhibitor, calcium channel blocker, beta-blocker.

<sup>b</sup>Lifestyle strategies should be recommended regardless of the risk category: 1. No smoking, 2. Healthy diet (total fat <30% of calories, saturated fat < 10% of calories, trans-fatty acids intake should be reduced as much as possible or eliminated and most dietary fat should be polyunsaturated, daily salt intake <5 g or <90 mmol, at least 400 g a day of a range of fruits and vegetables as well as whole grains and pulses). 3. At least 30 minutes of moderate physical activity (e.g., brisk walking) a day, through leisure time, daily tasks, and work-related physical activity. 4. Weight control. 5. Reduced alcohol consumption (<3 unit of alcohol per day: one unit (drink) = half pint of beer/lager (5 % alcohol), 100 ml of wine (10 % alcohol), spirits 25 ml (40% alcohol).

### PROCAM

Among the other systems available for calibrating risk are the PROCAM (PROspective Cardiovascular Münster) Quick Check and Health Check systems.<sup>28</sup> The PROCAM systems provide an estimate of the risk for cardiovascular events, limited here to myocardial infarction (both fatal and nonfatal) and sudden coronary death, for men and women aged 20-75 years. The development of the score was based on data from more than 25,000 subjects in Germany who were followed up to 22 years, and it is tailored to a European population.<sup>29</sup> The

PROCAM Quick Check allows an initial assessment of coronary risk without laboratory testing, while the PROCAM Health Check includes laboratory values (low-density lipoprotein cholesterol [LDL-C], HDL-C, triglycerides, and blood glucose). The PROCAM risk assessment tools are recommended for use in the guidelines developed by the International Task Force for Prevention of Coronary Heart Disease and can be found at: [http://www.chd-taskforce.com/coronary\\_risk\\_assessment.html](http://www.chd-taskforce.com/coronary_risk_assessment.html).

### Table 2. Management of high low-density lipoprotein levels according to National Cholesterol Education Program Adult Treatment Panel III, the US

Step 1: Risk estimation using electronic 10-year risk calculators that are available at [www.nhlbi.nih.gov/guidelines/cholesterol](http://www.nhlbi.nih.gov/guidelines/cholesterol); Third report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): executive summary [October 16, 2008]. Accessed April 20, 2010.

Step 2: Clinical management:

Risk category (10-year risk of myocardial infarction and coronary death) <sup>a</sup>	LDL-C goal (in mg/dL)	Therapeutic lifestyle changes (LDL-C in mg/dL) <sup>b</sup>	Drug therapy (LDL-C in mg/dL) <sup>c</sup>
<b>High:</b>  CHD or CHD equivalents <sup>d</sup> or calculated risk >20% among persons without history of CHD or CHD equivalents	<100 (optional goal: ≤70)	≥100	≥100 (<100: consider drug options)
<b>Moderately high:</b>  ≥2 risk factors <sup>e</sup> (risk 10%-20%)	<130	≥130	≥130 (100-129: consider drug options)
<b>Moderate:</b>  ≥2 risk factors <sup>e</sup> (risk ≤ 10%)	<130	≥130	≥160
<b>Low:</b>  ≤1 risk factor <sup>f</sup>	<160	≥160	≥190 (160-189: LDL-C-lowering drug optional)

**Abbreviations:** CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol.

<sup>a</sup> Risk categories according to National Cholesterol Education Program Adult Treatment Panel III.

<sup>b</sup> For persons at high or moderately high risk with lifestyle-related risk factors (e.g., obesity, physical inactivity, elevated triglyceride, low high-density lipoprotein cholesterol [HDL-C], or metabolic syndrome), regardless of LDL-C level.

<sup>c</sup> Drug therapy should be sufficient to achieve ≥30%-40% reduction in LDL-C levels.

<sup>d</sup> CHD includes history of myocardial infarction, unstable angina, stable angina, coronary artery procedures (angioplasty or bypass surgery), or evidence of clinically significant myocardial ischemia. CHD equivalents include clinical manifestations of noncoronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease [transient ischemic attacks or stroke of carotid origin or >50% obstruction of a carotid artery]), diabetes, and ≥2 risk factors with 10-year risk for CHD >20%.

<sup>e</sup> Risk factors include cigarette smoking, hypertension (blood pressure ≥140/90 mm Hg or taking antihypertensive drug), low HDL-C (<40 mg/dL), family history of premature CHD (CHD in male first-degree relative <55 years of age; CHD in female first-degree relative <65 years of age), and age (men ≥45 years; women ≥55 years).

<sup>f</sup> Most persons with ≤1 risk factor have a 10-year risk <10%, indicating that a 10-year risk assessment for such persons is unnecessary.

### Limitations of the Guidelines Incorporating the Global CVD Risk Assessments and Alternative Approaches

Recently, several concerns were raised about the guidelines incorporating the total CVD risk assessments.<sup>5,30,31</sup> First, the

CVD risk estimation systems are based on mathematical equations that differ in the thresholds for indicating high risk and in the population used as a base, the age ranges, and the sample sizes of the datasets.<sup>31</sup> Second, the number of risk factors and the baseline risk in the population being examined can influence the accuracy of estimation, as can the



end points chosen (events vs. deaths, CHD vs. CVD, etc.).<sup>31</sup> For example, using the Framingham system the risk is overestimated if baseline risk is low and underestimated if it is high.<sup>5</sup> Third, errors in the population's parameters and in patient measurements may decrease the precision of the estimate. In fact, a 30% risk that is calculated by the Framingham equation and based on a single lipid measurement should actually be expressed as ranging from 23% to 37% to account for a lack of precision.<sup>31</sup> It has been recognized that some guidelines may be difficult to use in

everyday clinical practice. The recent study from the US showed that management of high blood cholesterol incorporating the Framingham system remains suboptimal.<sup>32</sup> Finally, only limited research is available to support the conclusion that clinical outcomes improve with an introduction of such clinical guidelines.<sup>5</sup> For example, in a recent systematic evidence-based review of 18 studies (14 of them were clinical trials), total CHD risk information alone or with accompanying education increased the probability to initiate intervention in moderate to high risk patients.

**Table 3.** Management of CVD risk factors based on the European guidelines on preventing cardiovascular disease in clinical practice.

Step 1: Risk estimation using SCORE system: <http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/cvd-prevention.aspx>. Accessed by April 10, 2010. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, et al. European guidelines on cardiovascular disease prevention in clinical practice: full text. Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts), Eur J Cardiovasc Prev Rehabil. 2007;14(Suppl 2):S1-S113.

Step 2: Clinical management:

Risk category (10-year risk of CVD death) <sup>a</sup>	Nicotine replacement therapy	Antihypertensive therapy <sup>b</sup>	Lipid-lowering therapy <sup>b</sup>	Antiplatelet therapy	Other targets and therapy
<b>Low: risk &lt;5%</b>	Nicotine replacement therapy and/or nortriptyline or amfebutamone (bupropion) should be offered to motivated smokers who fail to quit with counseling.	Blood pressure at $\geq 140/90$ mm Hg, if feasible.	Total cholesterol at or above 190 mg/dL (5 mmol/L) or  Low-density lipoprotein cholesterol at 115 mg/dL (3 mmol/L).		
<b>High: existing CVD, or diabetes or risk <math>\geq 5\%</math></b>	Nicotine replacement therapy and/or nortriptyline or amfebutamone (bupropion) should be offered to motivated smokers who fail to quit with counseling.	Blood pressure at $\geq 130/80$ mm Hg, if feasible.	Total cholesterol at or above 175 mg/dL (4.5 mmol/L) or, if feasible, at 155 mg/dL (4.0 mmol/L).  Low-density lipoprotein cholesterol at 100 mg/dL (2.5 mmol/L) or if feasible, at 80 mg/dL (2.0 mmol/L).	Individuals with risk $\geq 10\%$ , existing CVD, or diabetes.	Diabetes: fasting blood glucose $< 6$ mmol/L ( $< 110$ mg/dL) and HbA1c $< 6.5\%$ if feasible.  Post-MI, angina, CHF: beta-blockers.  CHF, left ventricular dysfunction, diabetes with hypertension or nephropathy: ACE inhibitors.  History of thromboembolic events, left ventricular thrombus, atrial fibrillation: anticoagulants.  Large anterior MI, left ventricular aneurysm, paroxysmal tachyarrhythmias, post-MI CHF: consider anticoagulants.

**Abbreviations:** CVD: cardiovascular disease; MI: myocardial infarction; CHF: congestive heart failure; ACE: angiotensin-converting enzyme.

<sup>a</sup> Risk may be higher than indicated in the chart in sedentary or obese subjects, especially those with central obesity; those with a strong family history of premature CVD; the socially deprived; those with low HDL cholesterol (high-density lipoprotein cholesterol  $< 40$  mg/dL [1.0 mmol/L] for men and  $< 45$  mg/dL [1.2 mmol/L] for women) or elevated fasting triglycerides ( $\geq 150$  mg/dL [1.7 mmol/L]); asymptomatic subjects with evidence of preclinical atherosclerosis.

<sup>b</sup> Lifestyle strategies should be recommended regardless of the risk category (no smoking; healthy food choices; physical activity: 30 min of moderate activity a day; body mass index [in  $\text{kg}/\text{m}^2$ ]  $< 25$ ).

However, authors concluded that the effect of total risk assessment on long-term clinical outcomes including maintenance of therapies remains to be clarified.<sup>33</sup>

Both modified and alternative approaches to using the guidelines described in this paper have been suggested. One of these approaches is “a screen and diagnostic test protocol” in which Reynolds proposed applying the risk assessment as a first step (screening) to identify high- and intermediate-risk patients.<sup>31</sup> As a second step (diagnostic test) for deciding on treatment, additional tests with better reproducibility (e.g., an ultrasound to measure carotid intima-media thickness) would be conducted.<sup>31</sup> Gaziano M. and Gaziano T.<sup>21</sup> offered another approach, which involved simplification of the risk assessment system currently used in the US, by classifying all patients into only two strata: those for whom lipid-lowering therapy should be considered (these would be persons with known CVD and diabetes mellitus or who had a calculated risk of CHD 20% or more) and those for whom such therapy is not warranted. These authors stated that the lower the LDL-C levels the better and indicated that a 50% reduction in this level is a reasonable benchmark.

All CVD risk estimation systems described in this review include age, sex, smoking, blood pressure and lipids. To improve performance of these systems, the addition of other risk factors (socio-economic status, ethnicity, use of antihypertensive medications, C-reactive protein, genetic markers, etc.) to the models has been suggested.<sup>5</sup> It was found that only small improvement in risk prediction models was achieved by the addition of extra factors.<sup>5</sup> However, this may be debatable since the statistical methods, which used to evaluate the contribution of the additional risk factors, have limitations.<sup>34</sup> To overcome the shortcomings of the old methods, several newly proposed methods are currently available.<sup>34</sup>

The fourth approach, recently suggested by Hingorani and Psaty, is to offer generic statins to all adults based on an age threshold irrespective of their level of LDL-C, CRP, or absolute risk.<sup>35</sup> As 96% of all CVD events occur in persons older than age 55, the authors indicated that that age can be used as the threshold. The authors also noted the possibility of using a polypill (combines lipid-lowering medication and an agent to lower blood pressure) in this age group. A recent meta-analysis that included 464,000 participants from more than 150 clinical trials also supports the simplification of guidelines on the use of drugs for lowering blood pressure and for treating high blood pressure in everyone over a certain age.<sup>36</sup> This meta-analysis found that the reduction in CVD events was similar regardless of the type of medication (thiazides, beta blockers, angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers, or calcium channel blockers), the pretreatment blood pressure, and the presence or absence of existing CVD. In view of the large number of assumptions used to draw these conclusions, the possibility of side-effects, undetermined cost-efficiency, and unknown applicability in clinical practice, caution should be used in interpreting or applying the results.

### World perspective of risk assessment and management

Levels of mortality from stroke and CHD vary widely by country, with national per capita income being the strongest predictor of mortality even after adjustment for CVD risk factors.<sup>37</sup> The age-standardized death rates reported by the WHO are generally 1.5-4.0 and 2.0-5.0 times as high for CHD and stroke, respectively, in countries with low or mid-level incomes as they are in Japan or non-Asian high-income countries.<sup>38</sup> Compared with Western countries, China, Korea, and Thailand all have a higher incidence of stroke and of stroke mortality but a lower incidence of CHD and lower CHD mortality.<sup>38</sup> The evidence obtained from large epidemiological studies, including the Asia Pacific Cohort Study Collaboration and the Seven Countries Study, has revealed that the risk factors for CVD and the direction of their associations with outcomes for this disease are similar in different parts of the world.<sup>39-43</sup> Fortunately, increased efforts to prevent, diagnose, and treat ischemic heart disease and stroke during the last several decades led to a substantial reduction in CVD mortality in Western Europe, North America (excluding Mexico), Japan, Australia, and New Zealand.<sup>44</sup> For example, in Japan, a country whose mortality rate from stroke was the highest of any country included in the WHO death database in 1965, a reduction in the smoking rate, the decline in blood pressure at the population level, and a decrease in the prevalence of hypertension led to a substantial (70%) reduction in stroke mortality from 1965 to 1990.<sup>11</sup> In a study by Ford and colleagues in the US, the authors estimated that 47% of the reduction in expected CHD deaths from 1980 to 2000 was due to the use of medical treatments (therapy for heart failure, secondary prevention, treatment for acute coronary syndrome, and primary prevention with statins).<sup>12</sup> The decrease in the prevalence of risk factors (smoking, high blood pressure, and high total cholesterol) at population level accounted for 44% of this reduction.<sup>12</sup>

Even in the US and other high-income countries, there is a substantial potential for improving the identification and treatment of high-risk patients. In the US, for example, the prevalence of high LDL-C levels, a primary target for cholesterol management recommended by the NCEP (National Cholesterol Education Program) ATP III decreased from 32% in 1999 to 21% in 2006. Perhaps about half of this decrease was due to an increase in the use of lipid-lowering medication.<sup>32</sup> Even so, in the US in 2005-2006 about 35% of persons with high LDL-C levels were unscreened, approximately 25% were undiagnosed, and about 40% were untreated or inadequately treated.<sup>32</sup> Moreover, among those at high risk for CHD over the course of 10 years, about two-thirds were eligible for lipid-lowering drug therapy but were not receiving it during the period in question.<sup>32</sup> Poor access to health care, lack of awareness among clinicians of the current guidelines, their failure to adhere to these guidelines, and failure of patients to comply with recommended therapeutic lifestyle changes and prescribed medication have been suggested as factors contributing to the high prevalence of elevated LDL-C in the US.<sup>45-47</sup>

The problem of a gap in treatment is even bigger in middle- or low-income countries. In many of these countries, the reported prevalence of abnormal lipid levels, smoking, and high blood pressure is already high and continues to increase.<sup>48,49</sup> For example, according to the global burden of disease database for countries in WHO's Southeast Asia subregion where mortality for both children and adults is high (Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Maldives, Myanmar, and Nepal), the burden of disease attributable to each of CVD risk factor (tobacco, blood pressure, and cholesterol) in 2000 already had a magnitude comparable to deficiencies in intake of micronutrients or indoor smoke from solid fuels or 3 other environmental risks (poor water, sanitation, and hygiene).<sup>50</sup> According to the results of Prevention of REcurrences of Myocardial Infarction and Stroke WHO study (WHO-PREMISE) in 10 developing countries (Brazil, Egypt, India, Indonesia, Islamic Republic of Iran, Pakistan, Russian Federation, Sri Lanka, Tunisia and Turkey), less than one-fifth of all patients with a previous history of CVD were taking lipid-lowering medications.<sup>51</sup> The reported prevalence of high blood pressure in the Asia-Pacific Cohort Studies Collaboration study is comparable to that in Western countries, but a large proportion of deaths from CVD is attributable to hypertension.<sup>52,53</sup> Poor management of hypertension may be one of the major factors contributing to the disparity in CVD mortality between low-middle and high income regions. The prevalence of high blood pressure varies widely by location while rates of awareness, treatment, and control are low in China.<sup>54-56</sup> To illustrate, in a large representative study in rural Shandong Province, China, the prevalence of hypertension was high (43.8%). Only 26.2%, 22.2%, and 3.9% of hypertensive patients were aware of their hypertension, were currently taking antihypertensives, and had achieved control of their blood pressure, respectively.<sup>56</sup> In another population-based study of rural Chinese adults, the prevalence of blood pressure control was even lower (1.5%).<sup>55</sup> In a recent study of rural residents and 921 urban residents in China, given the current annual cost of antihypertensive drugs (500 Ren Min Bi (RMB) or US\$73.3 as of 8 May 2009) participants, on average, were willing to pay for the drugs only when the 5-year cardiovascular disease risk was 35% higher.<sup>57</sup> The barriers interfering with control of risk factors for CVD in middle- and low-income settings are similar to those in high-income settings but probably on a larger magnitude. The limited availability of health care providers, budgetary constraints for the majority of population, and the problem that drugs are not in stock are additional factors contributing to poor control of CVD risk factors in middle- and low-income countries.<sup>58</sup>

## Conclusion

A substantial decrease in the burden of CVD could be achievable using the low-risk population approach and the strategy aimed at high-risk individuals. To address the clinical management of CVD risk factors at the individual level various practice guidelines have been developed by major medical organizations. The use of the clinical guidelines that integrate the assessment of total risk of

developing CVD during the next 5 or 10 years has some limitations and challenges. Alternative or modified approaches for the management of CVD risk factors have been discussed in this report. They include: 1) use of risk estimation as a screening tool for identifying high-/intermediate-risk patients who should undergo additional diagnostic tests (e.g., ultrasound for subclinical atherosclerosis), 2) measurement of newer markers such as high-sensitivity C-reactive protein, 3) simplification of the CVD risk assessment for identifying patients who are candidates for therapy with decreasing the level of risk factors relatively to the baseline's level where treatment is offered, and 4) initiation of drug therapy after a certain age threshold. Future studies are needed to evaluate the effectiveness of these identified strategies.

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None reported.

## Disclaimer

The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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