MINISTRY OF HEALTH
SINGAPORE

Screening for Cardiovascular Disease and Risk Factors

MOH Clinical Practice Guidelines 1/2011

College of Family Physicians, Singapore

Academy of Medicine, Singapore

Singapore Heart Foundation
Your Heart ... We Care

Clinical Neuroscience Society, Singapore

Chapter of Public Health & Occupational Physicians, Academy of Medicine, Singapore

Chapter of Cardiologists College of Physicians, Singapore

College of Radiologists, Singapore

Singapore Medical Association

Singapore Cardiac Society

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Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
1^{++}	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1^{+}	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2^{++}	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1^{++} and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1^{++} or 1^{+}
C	A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2^{++}
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2^{+}
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group

CLINICAL PRACTICE GUIDELINES

Screening for Cardiovascular Disease and Risk Factors

MOH Clinical Practice Guidelines 1/2011

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Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Such standards are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

Contents

Foreword

Cardiovascular disease is a leading cause of morbidity and mortality worldwide. In 2008, ischaemic heart disease and cerebrovascular disease accounted for 3.5% and 2.1% of all hospital discharges; and 20.1%, and 8.3% of total causes of death respectively in Singapore.

Cardiovascular disease is a continuum that begins with the lifestyle factors of smoking, physical inactivity, and atherogenic diet, progressing to high risk diseases of hypertension, diabetes, dyslipidemia, and obesity. These in turn proceed via progressive vascular disease to target organ damage, end-organ failure and mortality.

Intervention anywhere along this disease continuum could disrupt the pathophysiological process and thus confer cardiovascular protection. Also, since many cardiovascular events share the same etiology, assessing and treating a patient's overall cardiovascular risk should be emphasized rather than treating risk factors in isolation.

Appropriate screening of asymptomatic individuals who have modifiable risk factors, followed by explanation, counselling, and intervention remain the most cost-effective way to reduce future disease burden, suffering and health care costs. Health screening is incomplete without patient counselling and recommendations for therapeutic lifestyle changes by the patient. It is also important that tests with recommendations against their use be avoided.

This set of clinical practice guidelines updates the topics in the 2003 edition of the MOH health screening related to cardiovascular disease and risk factors. It also provides guidance on the use of new cardiovascular biomarkers, Pre-participation screening for exercise, screening of asymptomatic cardiovascular disease in diabetes mellitus, chronic renal disease, abdominal aortic aneurysm, peripheral vascular disease, cerebrovascular disease, and atrial fibrillation.

I would like to commend the workgroup for their contributions. It is hoped that these guidelines will assist medical practitioners in their clinical practice.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES

Executive summary of key recommendations

This Executive Summary lists the recommendations in this CPG on the screening of cardiovascular disease and risk factors. Details of the recommendations listed can be found in the main text as the pages indicated.

Screening for cardiovascular risk factors

B All patients should be asked if they use tobacco and their smoking status be documented on a regular basis (pg 14).

Grade B, Level 2+

B Consistent update of smoking cessation status of every tobacco user is recommended at each clinical consultation (pg 15).

Grade B, Level 2+

D All patients aged 18 and older should be asked if they are participating in any physical activity and if so, the level, intensity and duration, of such activity (pg 15).

Grade D, Level 4

D It is recommended that each individual be screened for adherence to the Singapore Health Promotion Board's guidelines for healthy eating (pg 16).

Grade D, Level 4

C It is recommended that screening for obesity be done for individuals 18 years and older annually. The height, weight and waist circumference should be measured and the body mass index be calculated (pg 16).

Grade C, Level 2+

B It is strongly recommended that clinicians routinely screen men and women aged 40 years and older for lipid disorders (pg 18).

Grade B, Level 2++

GPP It is recommended that clinicians routinely screen younger adults (men and women aged 18 and older) for lipid disorders if they have other risk factors for coronary artery disease (pg 18).

GPP

GPP It is recommended that clinicians review patients' lipid levels at regular levels depending on the risk categories and whether on lipid modifying drug therapy (pg 19).

GPP

D Periodic screening for hypertension is recommended for all adults aged 18 years or older. Blood pressure should be measured at least once every 2 years for individuals with diastolic pressure below 80 mmHg and a systolic pressure below 130 mmHg (i.e. normal blood pressure). Measurements are recommended annually for persons with a diastolic blood of 80-89 mmHg or systolic blood pressure of 130-139 mmHg (i.e. high normal blood pressure). Persons with higher blood pressures or a major coronary risk factor such as diabetes mellitus require more frequent measurement (pg 19).

Grade D, Level 4

D The following procedures are recommended when recording BP:

- Allow the patient to sit or lie down for several minutes before measuring the BP.
- The patient should refrain from smoking or ingesting caffeine during the 30 minutes preceding the measurement.
- Use a cuff with a bladder that is 12-13 cm X 35 cm in size, with a larger bladder for fat arms. The bladder within the cuff should encircle at least 80% of the arm.
- Use the disappearance of phase V Korotkoff sound to measure the diastolic BP.
- Measure the BP in both arms at the first visit.
- Take 2 or more readings separated by 2 minutes. Average these 2 values. If the first 2 readings differ by more than 5 mmHg, additional readings should be obtained and averaged.
- Measure the BP in both the standing and supine position for elderly subjects and diabetic patients.
- Place the sphygmomanometer cuff at the heart level, whatever the position of the patient.

(pg 19) **Grade D, Level 4**

D Screening of asymptomatic individuals for type 2 diabetes mellitus should be carried out on an opportunistic basis. Testing should be considered in adults of any age who have one or more risk factors for diabetes. In those without risk factors, testing should begin at 40 years (pg 21).

Grade D, Level 4

D When screening for diabetes mellitus, fasting plasma glucose should be used. If the blood cannot be processed within 60minutes, the blood should be placed in a tube containing sodium fluoride (pg 21).

Grade D, Level 3

B In patients with typical symptoms, diabetes mellitus can be diagnosed if any one of the following is present:

Casual[b,c] plasma glucose	> 11.1 mmol/L
Fasting[d,e] plasma glucose	> 7.0 mmol/L
2h plasma glucose during oral glucose tolerance testf	> 11.1 mmol/L

a. where the diagnostic criterion is met in the absence of typical symptoms, a second confirmatory test should be performed on another day.
b. casual is defined as any time of day without regard to interval since last meal
c. fasting is defined as no caloric intake for at least 8 hours
d. fasting plasma glucose is the more convenient screening test when compared to the glucose tolerance test
e. Subjects with fasting glucose from 6.1 to 6.9 mmol/L should undergo an oral glucose tolerance test
f. 75 g oral glucose tolerance test should be performed according to WHO recommendations.

(pg 22)

Grade B, Level 2++

GPP It is recommended that HbA1c not be used as a screening and diagnostic tool for diabetes mellitus until its performance in our multi-ethnic population has been evaluated (pg 22).

GPP

Screening for asymptomatic coronary artery disease

C In asymptomatic individuals it is recommended that the risk of cardiovascular disease first be estimated based on the global assessment of risk factors (pg 26).

Grade C, Level 2+

D The Framingham Risk Score adapted to the Singapore population should be used to give an estimate of an individual's risk of major coronary artery disease events (pg 27).

Grade D, Level 4

A People with diabetes should no longer be automatically assigned to the high risk category for cardiovascular risk. They should therefore be based on appropriate patients' coronary artery disease risk estimates (pg 27).

Grade A, Level 1++

C In low risk individuals (<10% 10-year risk of coronary artery disease) further testing for coronary artery disease is not routinely recommended (pg 28).

Grade C, Level 2++

C There is insufficient evidence to recommend for or against routine screening for coronary artery disease in asymptomatic individuals with intermediate (10-20% 10-year risk of coronary artery disease) or high risk (>20% 10-year risk of coronary artery disease). Given the lack of evidence, in intermediate and high risk asymptomatic individuals, further screening should be limited to the following selected situations:

- The exercise treadmill test (exercise treadmill testing) may be performed to: evaluate those with multiple risk factors as a guide to risk-reduction therapy; evaluate asymptomatic men older than 45 years of age and women older than 55 years of age who plan to start vigorous exercise, are involved in occupations in which impairment might impact public safety, or are at high risk for coronary artery disease because of other diseases; evaluate asymptomatic persons with diabetes who plan to start vigorous exercise.

- The coronary calcium score (CACS) on electron-beam computed tomography may be used in the intermediate coronary artery disease risk patient to decide if the patient should be reclassified to a higher risk status based on a high CACS.
  (pg 29)

Grace C, Level 2++

B The routine use of the resting ECG for screening for coronary artery disease in asymptomatic individuals is not recommended (pg 29).

Grade B, Level 2++

B Routine use of the exercise treadmill testing to screen for coronary artery disease in asymptomatic low-to-moderate risk individuals is not recommended. Its use among those in the highest risk group (10-year predicted coronary artery disease risk of 20%) may be considered (pg 30).

Grade B, Level 2++

D Cardiac stress imaging is not recommended for routine screening for coronary artery disease in asymptomatic patients at low risk (pg 31).

Grade D, Level 4

D Cardiac stress imaging or stress echocardiography may be considered in a patient who has moderate to high risk of coronary artery disease and abnormal exercise ECG (pg 32).

Grade D, Level 4

D Stress imaging is not useful for patients with no clinical risk factors who are undergoing intermediate-risk non-cardiac surgery. Such testing is also not useful for asymptomatic patients undergoing low-risk non-cardiac surgery (pg 33).

Grade D, Level 4

D Cardiac stress imaging may be considered as pre-operative screening in asymptomatic individuals prior to non-cardiac surgery whose: (a) functional status is poor (less than 4 Mets) or unknown, (b) undergoing vascular surgery or intermediate risk surgery (intra-peritoneal and intra-thoracic surgery, carotid endarterectomy, head and neck surgery, orthopaedic surgery, prostate surgery) with (c) 1 or more risk factors (history of heart disease, history of compensated or prior heart failure, history of cerebrovascular disease, diabetes mellitus, or renal insufficiency) and (d) in whom the results of testing will change management (pg 34).

Grade D, Level 4

D The use of coronary artery calcium score (CACS) by means of computerised tomography may be considered in selected situations, namely:

- asymptomatic patients with intermediate coronary artery disease risk (between 10% and 20% 10-year risk of estimated coronary events, based on the possibility that such patients might be reclassified to a higher risk status based on high CACS, and subsequent patient management may be modified,

- patients who have atypical cardiac symptoms but otherwise considered to be at low risk of coronary disease, who may benefit from CACS to help in ruling out the presence of obstructive coronary disease.

(pg 34) **Grade D, Level 4**

D Use of CT coronary angiography as a screening test in low- and intermediate-risk asymptomatic persons is not recommended (pg 36).

Grade D, Level 4

C Carotid intima-media thickness measurement is not recommended for routine cardiovascular disease screening (pg 37).

Grade C, Level 2+

D It is recommended that the ankle brachial index (ABI) be considered as a screening test for individuals with high risk for peripheral vascular disease, namely

- Age less than 50 years, with diabetes and one other atherosclerosis risk factor (smoking, dyslipidemia, or hypertension).
- Age 50-69 years and history of smoking or diabetes.
- Age 70 years and older.

(pg 39) **Grade D, Level 4**

B The ankle brachial index may be considered for purpose of reclassification of an individual who has intermediate risk of coronary artery disease (pg 39).

Grade B, Level 2+

Biochemical tests in cardiovascular screening

GPP For lipid screening, it is recommended that testing be carried out on a venous sample sent for laboratory analysis and not from a finger-prick capillary sample tested on a physician office or bedside testing device (pg 41).

GPP

B For lipid screening, it is recommended that a fasting venous sample should be collected for lipid levels of total cholesterol, triglycerides, high density lipoprotein cholesterol (HDL-C). The low density lipoprotein cholesterol (LDL-C) can be reported as a calculated value or as a directly measured result (pg 41).

Grade B, Level 2++

B Lipoprotein(a) determination is not recommended for routine cardiovascular screening (pg 42).

Grade B, Level 2++

C Further to a global cardiovascular risk assessment, lipoprotein(a) measurements may be useful in individuals with a strong family history of premature cardiovascular disease (pg 43).

Grade C, Level 2+

D Routine apolipoprotein B determination is not recommended (pg 43).

Grade D, Level 4

C It is recommended that caution be exercised in the application of high sensitivity C-reactive protein as a screening test as risk prediction is not established in Asians and in the elderly (pg 43).

Grade C, Level 2+

B The measurement of high sensitivity C-reactive protein is recommended only if the 10-year predicted risk based on standard global risk assessment is 5% or more (pg 44).

Grade B, Level 2+

GPP If the high sensitivity CRP concentration is <3 mg/L, it does not need to be repeated. If the value is >3 mg/L, repeat the measurement at least 2 weeks later with patient in stable state, free of infection or acute illness. Select the lower of the 2 results as the patient's value (pg 44).

GPP

GPP Plasma homocysteine measurement is not recommended in cardiovascular screening (pg 44).

GPP

B Fibrinogen measurement is not recommended for cardiovascular disease screening (pg 45).

Grade B, Level 2++

B Natriuretic peptides (BNP and NT-proBNP) measurement is not recommended for cardiovascular disease screening (pg 45).

Grade B, Level 2++

Screening for asymptomatic cardiovascular disease in diabetes mellitus and chronic renal disease

D Global cardiovascular assessment is recommended for all patients with diabetes mellitus (pg 46).

Grade D, Level 4

D It is recommended that the assessment of cardiovascular risk in persons with type 2 diabetes mellitus include a medical history, physical examination, blood pressure, fasting serum lipids, assessment of urine for microalbuminuria or proteinuria, and a resting ECG at baseline (pg 47).

Grade D, Level 4

D For asymptomatic individuals with diabetes above 40 years of age and intending to engage in more than low intensity exercise, a pre-exercise evaluation and a graded exercise stress ECG are recommended (pg 48).

Grade D, Level 4

D In patients at risk of chronic kidney disease, screening for risk factors for cardiovascular disease and for coronary artery disease is recommended at baseline and when patients become symptomatic of renal disease (pg 49).

Grade D, Level 4

D Since the single most important determinant of cardiovascular disease burden is the severity of chronic kidney disease, screening for the presence and level of renal impairment is recommended (pg 49).

Grade D, Level 4

Screening for abdominal aortic aneurysm, peripheral arterial disease, cerebrovascular disease and atrial fibrillation

B Routine ultrasonographic screening of men 65 years and older for abdominal aortic aneurysm may be considered, particularly in those who have ever smoked (current and former smokers) (pg 52).

Grade B, Level 2++

B Routine screening for abdominal aortic aneurysm in women is not recommended (pg 52).

Grade B, Level 2+

D Routine screening for carotid artery stenosis is not recommended (pg 53).

Grade D, Level 4

GPP Routine screening for cerebrovascular disease by MRI is not recommended (pg 54).

GPP

B Opportunistic screening for atrial fibrillation should be routinely performed for all patients by examining the rate and rhythm by pulse palpation, followed by ECG if atrial fibrillation is suspected (pg 54).

Grade B, Level 2++

Pre-participation screening for exercise

D Pre-participation screening should be done on risk-stratified groups of athletes (pg 58).

Grade D, Level 4

D All sports participants and national athletes should preferably undergo an appropriate level of annual pre-participation screening (pg 60).

Grade D, Level 4

D Sports participants involved in strenuous sporting activities, but at a less competitive level than national atheletes, should be encouraged to undergo voluntary pre-participation screening (pg 60).

Grade D, Level 4

D Participants in sports and recreational activities should be encouraged to complete a self-administered pre-participation screening questionnaire annually, and consult a doctor if the questionnaire indicates it (pg 61)

Grade D, Level 4

D For pre-participation screening, a two- or more stage screening process is encouraged, where the first stage consists of personal and family history taking and physical examination. Based on the findings of the first stage, further tests such as a resting ECG (if not already done), chest X-ray, exercise stress test, echocardiogram, blood investigations, urine tests, etc. may be ordered if indicated (pg 61).

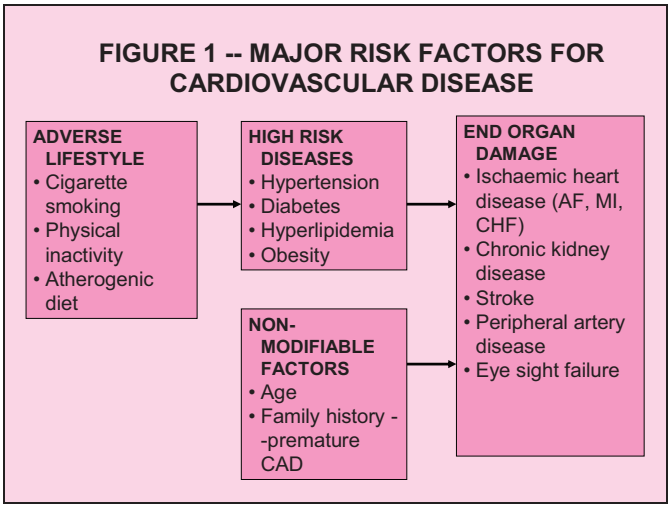
Grade D, Level 4

GPP Abbreviated screening protocols are acceptable in the intervening years between the full screening (pg 61).

GPP

1 Introduction

Recommendations on screening for dyslipidemia, hypertension, diabetes mellitus, and obesity published in the 2003 edition of the MOH clinical practice guideline on health screening are updated in this guideline. Related topics on screening for cardiovascular disease namely, the emerging cardiovascular risk factors, Pre-participation screening for exercise, asymptomatic cardiovascular disease in diabetes and chronic renal disease, as well as screening for abdominal aortic aneurysm, peripheral artery disease, cerebrovascular disease, and atrial fibrillation are also included. See Appendix 1A and 1B regarding the accuracy and cost considerations respectively in deciding on the most appropriate screening tools.



The burden of cardiovascular disease in Singapore is sizeable. Cardiovascular diseases represent the largest category of diseases for which disability adjusted life-years (DALYs) are lost, accounting for 19.7% of all DALYs lost in Singapore in 2004. Of these, ischaemic heart disease (IHD) and stroke contributed to 10.2%, and 7.1% of the DALYs lost respectively.1 Coronary artery disease (CAD) and cerebrovascular disease contributed to 20.1%, and 8.3% of all deaths respectively in 2008.2 These two conditions accounted for 3.5%, and 2.1% of all hospital discharges in that year.[3]

Risk of cardiovascular disease is a continuum that begins with the presence of lifestyle related and inborn cardiovascular risk factors and progresses through vascular disease caused by these risk factors on to target organ damage and end-organ failure (cardiac, brain, kidney, eye, and peripheral vascular disease), and death.[4-5]

Appropriate screening for modifiable cardiovascular lifestyle risk factors and high risk diseases provide the information for timely intervention to disrupt the progression from risk to disease burden. (Figure 1).

Lifestyle change and where necessary, early treatment of high risk diseases combined with therapeutic lifestyle changes will reduce end organ damage.[6-7]

The contribution of the various risk factors for cardiovascular disease are revealed in the INTERHEART study a large standardised case-controlled study of acute myocardial infarction in 52 low- and middle-income countries. Important harmful factors (increase risk) that influence the risk of acute myocardial infarction in decreasing order are: dyslipidemia, smoking diabetes, hypertension, and abdominal obesity. The important protective factors (decrease risk) are daily fruit and vegetable consumption, and regular physical exercise (Table 1 on page 12).[8]

Single high risk factors are important in preventing cardiovascular disease, but the combined effect of many moderately high risk factors may be just as destructive as a single high risk factor – hence the need for a global risk assessment.

Table 1 Factors that influence the risk of acute myocardial infarction

Risk factor	Odds ratio (95% CI)
Harmful (increase risk)	
Dyslipidema (highest vs lowest decile)	3.25(2.81-3.76)
Smoking (current vs never)	2.87(2.58-3.19)
Diabetes	2.37(2.07-2.71)
Hypertension	1.91(1.74-2.10)
Abdominal obesity (highest vs lowest tertiles)	1.62(1.45-1.80)
Protective (decrease risk)	
Daily fruit and vegetable consumption	0.70 (0.62-0.70)
Regular physical exercise	0.86(0.76-0.97)

Source: Yusuf et al, 2004, the INTERHEART study.[8]

For global assessment of cardiovascular risk, the Framingham risk score is the prototype risk scoring system.[9] A comprehensive assessment of risk factors is recommended by the American Heart Association to be performed at least every 5 years starting at 18 years of age. Those with increased cardiovascular risk, for example, those with diabetes, cigarette smoker, or those with obesity, should have their risk factors and cardiovascular risk assessed more frequently.[10]

The Framingham risk score has been modified locally taking into account the Singapore cardiovascular epidemiological data. This modification was carried out as part of a collaboration between investigators at the Singapore Ministry of Health, Singapore General Hospital, National University of Singapore and Prof Ralph B D'Agostino from the Framingham Heart Study, USA.[11]

Based on the Framingham risk score, the individual is classified as low, intermediate, or high risk for cardiovascular disease corresponding respectively to a < 10%, 10 to 20% and > 20% risk of vascular events over a 10-year period, including non-fatal myocardial infarction or cardiac death.

For individuals at intermediate risk, the ability of emerging risk factors for coronary artery disease in further stratifying patients into high risk category have been evaluated by the United States Preventive Services

Task Force but none of the following have been shown conclusively to be suitable for routine use: (1) high-sensitivity C-reactive protein, (2) ankle-brachial index, (3) leukocyte count, (4) fasting blood glucose, (5) periodontal disease, (6) carotid intima-media thickness, (7) coronary artery calcium score on electron-beam computed tomography, (8) homocysteine level, and (9) lipoprotein(a) level.[12]

Finally, whilst the focus of this CPG is on screening for cardiovascular disease and risk factors, it is important to emphasise that the purpose of screening is to enable lifestyle interventions to be undertaken to reduce the burden of cardiovascular disease.

The recommendations in this CPG have also been categorized using the AMS-MOH Screening categories. Please see Appendix 4.

Review of guidelines

Evidence based clinical practice guidelines are by nature constantly evolving. New, emerging evidence could always supersede these guidelines and users need to be aware of this. The workgroup advises that these guidelines be scheduled for review in 3 years after publication or if it was felt that new evidence was available that would require substantive amendments to the current set of guidelines.

2 Screening for cardiovascular risk factors

2.1 Introduction

The focus of cardiovascular disease control has rightly shifted "upstream" to identify modifiable lifestyle factors for therapeutic lifestyle change, an important strategy in dealing with the cardiometabolic risk factors.

Screening for modifiable lifestyle habits namely smoking, physical inactivity, and atherogenic diet allows the opportunity for intervention to take place before the high risk diseases for cardiovascular disease develop, namely, hypertension, diabetes mellitus, hyperlipdemia, and obesity.

Healthy lifestyle habits should be recommended to everyone whether at high, moderate or low risk.

2.2 Smoking

The National Health Surveillance Survey (NHSS) 2007[13] showed 1 in 7 (13.6%) Singapore residents aged 18 to 69 years smoked cigarettes daily. The prevalence was Malays 23.2%, Chinese 12.3%, and Indians 11.4%. The proportion of male daily smokers was six times that of females (23.7% vs. 3.7%).

B All patients should be asked if they use tobacco and their smoking status be documented on a regular basis.[14-19]

Grade B, Level 2+

Tobacco use should be screened and documented on a regular basis. There is a relationship between the degree of exposure to smoking and the level of risk. Meta-analysis of five large, prospective, epidemiological studies found that the relative risk (RR) of ischaemic heart disease from smoking one cigarette per day was 1.39 (1.18-1.64 95% CI) increasing to 1.78 in subjects who smoked 20 cigarettes per day.[20-21]

Smoking cessation also reduces mortality in those who had an heart attack. A Cochrane review of 20 prospective cohort studies showed that smoking cessation results in 36% risk reduction in mortality (RR = 0.64; 95% CI, 0.58 to 0.71).[22]

B Consistent update of smoking cessation status of every tobacco user is recommended at each clinical consultation.[14-16]

Grade B, Level 2+

In screening for smoking cessation status, the steps in the 5As approach described in the MOH CPG on smoking cessation form a useful template for action. These steps are summarised below.[15, 23]

- Ask - for the smoking status of the individual.
- Advise - the individual to stop smoking if he is smoking.
- Assess - determine the individual's state of readiness to change.
- Assist - use motivational intervention, set a quit date, and assist the individual resolve any residual problems arising from quitting.
- Arrange follow-up - schedule subsequent follow up visits, preferably in person rather than via the telephone.

2.3 Physical activity

The National Health Surveillance Survey (NHSS) 2007 showed only 1 in 4 (23.6%) Singapore residents aged 18 to 69 years exercised regularly during their leisure time. The proportion was similar for males and females (25.1% vs 22.2%).

D All patients aged 18 and older should be asked if they are participating in any physical activity and if so, the level, intensity and duration, of such activity.[24]

Grade D, Level 4

Regular exercise of even moderate degree has a protective effect against coronary artery disease with 20-25% risk reduction. Vigorous physical activity will result in cardiac fitness.[24]

2.4 Diet

D It is recommended that each individual be screened for adherence to the Singapore Health Promotion Board's guidelines for healthy eating.[25]

Grade D, Level 4

Screening for healthy eating checks out the extent that the individual's diet is atherogenic. The adherence to the following guidelines as recommended by the Singapore Health Promotion in the document ABCs of healthy eating (www.hpb.gov.sg/personas/download.aspx?id=1344) is asked and recorded.[25]

- Eat 5 to 7 servings of rice and alternatives daily of which 2-3 servings are whole-grain products.
- Eat 2 servings of fruit and 2 servings of vegetables daily.
- Eat 2 to 3 servings of meat and alternatives daily of which ½ serving should come from dairy or other high calcium products.
- Use fats, oils and salt sparingly to flavour food.
- Include 6 to 8 glasses of fluid (1.5–2.0 litres) in the diet daily.

These guidelines are consistent with nutritional principles for prevention of cardiovascular disease summarised from the results of 147 epidemiological and dietary intervention studies.[26]

The Health Promotion Board guidelines are also consistent with the 2006 AHA dietary guidelines.[27]

2.5 Obesity

C It is recommended that screening for obesity be done for individuals 18 years and older annually. The height, weight and waist circumference should be measured and the body mass index be calculated.[28-30]

Grade C, Level 2+

Body mass index (BMI) is the recommended index to define overweight and obesity.[28-30] This measurement is useful for screening overweight and obesity because is minimally correlated with height, and highly correlated with body fat percentage and levels of disease risk of co-morbidities.

Based on body fat equivalence and co-morbid disease risk, BMIs of 23 and 27.5 kg/m^2 respectively have been recommended as cut-off points for public health action in Asians. See Table 2. This compares with the current WHO and international guidelines which recommend BMI cut-offs of 25 and 30 kg/m^2 to define overweight and obesity respectively.[28]

Table 2 BMI cut-off points for public health action in Asians (WHO 2004)

Cardiovascular disease risk	Asian BMI cut-off points for action (kg/m2)	Current WHO BMI cut-off points (kg/m2)
	<18.5	<18.5
Low	18.5 to 22.9	18.5 to 24.9
Moderate	23.0 to 27.4	25.0 to 29.9
High	27.5 to 32.4	30.0 to 34.9
Very high	32.5 to 37.4	35.0 to 39.9
	More or equal to 37.5	More or equal to 40.0

Source: MOH CPG on obesity, 2004 page 17[28]

Gender-specific waist circumference cut-offs should be used in conjunction with BMI to identify increased disease risk. Current international guidelines recommend waist circumference cut-offs of 102 and 88 cm to define excess risk for males and females respectively. Based on an Asian-Pacific consensus and the 2004 National Survey data and co-morbid disease risk, cut-offs of 90 and 80 cm respectively are recommended for Asians.[28]

Table 3 High risk gender-specific waist measurements thresholds (WPRO 2000)

Guideline	Waist circumference (cm) for Men	Waist circumference (cm) for Women
WHO, 1998	Equal or more than 102	Equal or more than 88
Asia-Pacific consensus	Equal or more than 90	Equal or more than 80

Source: MOH CPG on obesity, 2004 page 19[28]

Screening for BMI and waist circumference is useful because maintenance of a healthy body weight and waist circumference is recommended for non-hypertensive individuals to prevent hypertension and for hypertensive patients to reduce blood pressure. All overweight hypertensive patients should be advised to lose weight.[29]

2.6 Dyslipidemia

B It is strongly recommended that clinicians routinely screen men and women aged 40 years and older for lipid disorders.[31]

Grade B, Level 2++

The USPSTF found good evidence that screening for lipid disorders asymptomatic middle-aged people can identify people who are at increased risk of coronary artery disease. There is also good evidence that lipid-lowering drug therapy in such people substantially decreases the incidence of coronary artery disease with little major harm.[32]

The individual's cholesterol level contributes to the 10-year coronary artery disease risk score See Appendix 2A for men and Appendix 2B for women. This in turn allows classification of the patient into high (10-year coronary artery disease risk more than 20%), intermediate risk (10-year coronary artery disease risk 10-20%) or low cardiovascular risk (10-year coronary artery disease risk less than 10%).[11]

GPP It is recommended that clinicians routinely screen younger adults (men and women aged 18 and older) for lipid disorders if they have other risk factors for coronary artery disease.[11, 32]

GPP

Screening is recommended for men and women aged 18 and older in the presence of any of the following[11, 32]:

- Diabetes mellitus.
- A family history of cardiovascular disease before age 50 years in male relatives or age 60 years in female relatives.
- A family history suggestive of familial hyperlipidemia.
- Multiple coronary artery disease risk factors (e.g., tobacco use, hypertension).

GPP It is recommended that clinicians review patients' lipid levels at regular levels depending on the risk categories and whether on lipid modifying drug therapy.

GPP

2.7 Hypertension

D Periodic screening for hypertension is recommended for all adults aged 18 years or older. Blood pressure should be measured at least once every 2 years for individuals with diastolic pressure below 80 mmHg and a systolic pressure below 130 mmHg (i.e. normal blood pressure). Measurements are recommended annually for persons with a diastolic blood of 80-89 mmHg or systolic blood pressure of 130-139 mmHg (i.e. high normal blood pressure). Persons with higher blood pressures or a major coronary risk factor such as diabetes mellitus require more frequent measurement.[33-34]

Grade D, Level 4

Screening for hypertension is recommended for all adults aged 18 years and older and repeated every two years, annually, or more frequently depending on the initial blood pressure level or presence of major coronary risk factors.[35]

Since blood pressure is characterised by large spontaneous variations, it is important that the diagnosis of hypertension should be based on multiple blood pressure measurements taken on several separate occasions.

Evaluation of blood pressure

D The following procedures are recommended when recording BP:[33, 36-37]

- Allow the patient to sit or lie down for several minutes before measuring the BP.
- The patient should refrain from smoking or ingesting caffeine during the 30 minutes preceding the measurement.
- Use a cuff with a bladder that is 12-13 cm X 35 cm in size, with a larger bladder for fat arms. The bladder within the cuff should encircle at least 80% of the arm.

- Use the disappearance of phase V Korotkoff sound to measure the diastolic BP.
- Measure the BP in both arms at the first visit.
- Take 2 or more readings separated by 2 minutes. Average these 2 values. If the first 2 readings differ by more than 5 mmHg, additional readings should be obtained and averaged.
- Measure the BP in both the standing and supine position for elderly subjects and diabetic patients.
- Place the sphygmomanometer cuff at the heart level, whatever the position of the patient.

Grade D, Level 4

Grading hypertension

Hypertension is graded according to systolic and diastolic BP levels. See Table 4.[35]

Table 4 Definitions and classifications of BP levels for adults aged 18 years and older

Category	Systolic BP (mmHg)	Diastolic BP (mmHg)
Normal BP	<130	<80
High-Normal BP	130-139	80-89
Grade 1 Hypertension	140-159*	90-99
Grade 2 Hypertension	>160*	≥100
Isolated Systolic Hypertension*	≥140	<90
* Isolated systolic hypertension is graded according to the same level of systolic BP.		

Source: MOH CPG Hypertension 2/2005 page 13[35]

When the systolic and diastolic BP fall into different categories, the higher category should apply. For example, a BP of 162/92 mmHg should be Grade 2 Hypertension.[36]

2.8 Diabetes mellitus

Screening for diabetes mellitus in asymptomatic individuals

D Screening of asymptomatic individuals for type 2 diabetes mellitus should be carried out on an opportunistic basis. Testing should be considered in adults of any age who have one or more risk factors for diabetes. In those without risk factors, testing should begin at 40 years.

Grade D, Level 4

The risk factors [38] for diabetes are:

- overweight/obesity (BMI > 25.0 kg/m2)
- first-degree relative with diabetes
- high-risk race/ethnicity
- women who delivered a baby 4 kg or more; or were diagnosed with Gestational Diabetes Mellitus
- hypertension (>140/90 mmHg or on therapy for hypertension)
- HDL cholesterol level <1.0 mmol/L (male), <1.3 mmol/L (female) and/or a triglyceride level >2.2 mmol/L).
- women with polycystic ovarian syndrome (PCOS)
- IGT, or IFG on previous testing
- history of cardiovascular disease

If tests are normal, repeat testing at 3-year intervals is reasonable.

D When screening for diabetes mellitus, fasting plasma glucose should be used. If the blood cannot be processed within 60 minutes, the blood should be placed in a tube containing sodium fluoride.[39]

Grade D, Level 3

Glucometer readings are suitable for evaluation of glycemia control to evaluate adequacy of therapy only. Such readings should not be used for the screening for diabetes mellitus. Also, because plasma glucose will decline if the blood sample is not processed within 60 minutes of blood collection, a tube containing a glycolytic inhibitor such as sodium fluoride should be used for collecting the sample if the blood cannot be processed within 60 minutes.[39]

To reduce uncertainty, fasting plasma glucose is recommended over casual plasma glucose readings when screening for diabetes. Where casual plasma glucose readings are obtained opportunistically, the subject can only be categorised as unlikely to have diabetes if the level is < 6.0 mmol/L; or having diabetes if the level is > 11.1 mmol/L (with symptoms). Readings in between these two values would require a repeat fasting plasma glucose measurement.

B In patients with typical symptoms, diabetes mellitus can be diagnosed if any one of the following is present[40-41]:

Casual[b,c] plasma glucose	> 11.1 mmol/L
Fasting[d,e] plasma glucose	> 7.0 mmol/L
2h plasma glucose during oral glucose tolerance test[f]	> 11.1 mmol/L

a. where the diagnostic criterion is met in the absence of typical symptoms, a second confirmatory test should be performed on another day.
b. casual is defined as any time of day without regard to interval since last meal.
c fasting is defined as no caloric intake for at least 8 hours.
d fasting plasma glucose is the more convenient screening test when compared to the glucose tolerance test.
e Subjects with fasting glucose from 6.1 to 6.9 mmol/L should undergo an oral glucose tolerance test.
f 75 g oral glucose tolerance test should be performed according to WHO recommendations.[42]

Grade B, Level 2++

HbA1c for screening and diagnosis of diabetes mellitus needs further evaluation

GPP It is recommended that HbA1c not be used as a screening and diagnostic tool for diabetes mellitus until its performance in our multi-ethnic population has been evaluated.

GPP

Recently, the American Diabetes Association, based on recommendations by an International Expert Committee[43], has approved the use of glycated haemoglobin (HbA1c) as an additional alternative test which can be used in the screening and diagnosis of diabetes mellitus[44]. Although the HbA1c is a relatively convenient test which has been widely used as a measure of chronic glycemic exposure in people with diabetes, and has much strength, it is not without limitations[43, 45] and its performance as a screening and diagnostic tool in our local multi-ethnic population needs to be further evaluated before adoption.

3 Screening for asymptomatic coronary artery disease

3.1 Background

The concept of screening for coronary artery disease is highly popular, and intuitively very attractive. Many tests are available for diagnosis of coronary artery disease, and the public is well aware of many treatment options such as angioplasty and stenting, bypass surgery and medication. Screening in patients with increased risk may potentially be of benefit to those presumed to be at intermediate risk for coronary artery disease who could be reclassified as being at high risk (and thus benefit from more aggressive risk factor modification and/or coronary revascularisation if they are proven to have severe disease.

However, it is uncertain whether this increased yield of screening increases the detection of people with severe coronary artery disease to an important degree and whether invasive revascularization procedures would benefit those who are asymptomatic as much as those who have symptoms of coronary artery disease.[46-47] This uncertain benefit would need to be balanced against the possible harm from screening. Several challenges to effective screening for coronary artery disease exist, particularly in low risk asymptomatic individuals.

3.1.1 Diagnostic challenge

All our current tests for coronary artery disease detection involve a trade-off between accuracy, cost, radiation and invasiveness. The lowest cost tests generally have the least risk, e.g. treadmill ECG testing and also the lowest accuracy. The most accurate tests tend to be associated with higher risks such as radiation and invasiveness, while still not providing perfect accuracy. Judgment is needed.

Thus in a population with a low prevalence of disease, applying any test with limited accuracy, particularly limited specificity may yield a large number of false positive results, which may in turn generate further tests to exclude disease. The risks of non-invasive testing are very small, but in a low risk population, the benefits of detecting a few cases can easily be offset by the harm of widespread additional testing. For example, nuclear perfusion imaging or coronary angiography

to exclude coronary artery disease will expose a large number of individuals to radiation. Also a test may result in incidental findings which require further tests just to be sure that they are benign: a CT angiogram may reveal normal coronary arteries but also frequently "incidental" pulmonary nodules which because malignancy cannot be excluded confidently, lead to follow-up CT scanning to confirm that there is no progression of disease.

3.1.2 Treatment challenge

There is a common misperception that early detection of coronary artery disease is potentially lifesaving, because "prophylactic" angioplasty and stenting or bypass surgery will prevent a subsequent heart attack.

It is true that angioplasty can effectively control symptoms better than medication, and save lives in an acute heart attack situation. However, angioplasty has not been proven to prevent subsequent heart attacks in asymptomatic or even symptomatic patients with stable angina.

Similarly, randomised studies showing a survival benefit after bypass surgery for patients with chronic stable angina compared to medical therapy occurred in largely symptomatic patients (and only for patients with multi-vessel disease with impaired left ventricular function or left main disease). There is uncertainty whether revascularisation can improve survival in asymptomatic patients.

It could be argued that earlier detection of coronary artery disease would provide a basis for earlier implementation of preventive measures and medical therapies such as lifestyle modification, lipid lowering, and antiplatelet therapy. These therapies would have been applied anyway, depending on the patient's risk score.

It has also been proposed that tests such as calcium scoring that shift the patient from a lower risk category to a higher risk category and thereby alter the aggressiveness of lipid lowering, could be justified on these grounds. It must be noted, however, that even with detection of disease and aggressive lipid lowering, the risk of a cardiac event is only lowered, not eliminated. With recent recommendations for even lower target LDL cholesterol levels in lower risk individuals, the detection of coronary artery disease may not even be necessary for initiating more aggressive lipid lowering therapy.

3.1.3 Cost

Cost is frequently cited as the main reason why screening should not be advocated (and indeed, the costs of population screening would be enormous). Even if costs were not a consideration and the individual was willing to pay for a test, it should not be assumed that the benefits of screening will outweigh the risks. Ordering of screening tests must therefore be evidence based to ensure that wastage of resources and harm are kept to a minimum. Also to be cost effective, screening results need to be communicated to the individual screened and followed through interventions implemented. See Chapter 8 on cost effectivenesss issues.

3.1.4 Evidence from trials

Only a few randomized controlled trials have been performed to assess the value of screening for coronary artery disease, specifically in diabetics using myocardial perfusion imaging (DIAD)[48] and in pre-operative risk stratification (DECREASE II, DECREASE V).[49] The results from these randomized trials have not supported a role for unselective screening.

There is therefore little evidence to encourage routine screening for coronary artery disease in asymptomatic individuals. Based on the available expert opinion from published guidelines, screening for coronary artery disease should only be considered in specific circumstances listed below, after careful weighing of the risks and benefits in a given individual. The possible consequences of screening such as false positive or false negative results need for further testing and/or risks from radiation or stress should be explained to the subject prior to testing.

3.2 Global cardiovascular risk assessment

C In asymptomatic individuals it is recommended that the risk of cardiovascular disease first be estimated based on the global assessment of risk factors.[50-51]

Grade C, Level 2+

Single high risk factors are important in preventing cardiovascular disease, but the combined effect of many moderately high risk factors may be just as destructive as a single high risk factor. The global risk approach is therefore the first step in cardiovascular risk assessment. Thus, the following risk factors are included in the Framingham Risk Score as an example of a global risk assessment: age, gender, blood pressure or history of treatment for hypertension, smoking, elevated total cholesterol levels, and low level of high-density lipoproteins (HDL).[11, 50]

D The Framingham Risk Score adapted to the Singapore population should be used to give an estimate of an individual's risk of major coronary artery disease events.[9, 11]

Grade D, Level 4

These weightage of local risk factors has been incorporated into the Framingham risk score.[9, 11] The adapted Framingham risk scores are given in Appendix 2A and 2B, Other scores that have been applied include the European SCORE, PROCAM, ASSIGN, Reynolds risk score, and QRISK risk score. The risk QRISK2 is said to be most suitable for a European population.[52]

The Framingham Risk Score has been adapted to the Singapore population to give an estimate of an individual's risk of major coronary artery disease events, including myocardial infarction and coronary death.[11]

A People with diabetes should no longer be automatically assigned to the high risk category for cardiovascular risk. They should therefore be based on appropriate patients' coronary artery disease risk estimates.[53]

Grade A, Level 1++

The results of studies by Haffner[54] which concluded that diabetes is a coronary artery disease risk equivalent because it is associated with an absolute risk equivalent to that for recurrent major coronary events in patients with established coronary artery disease have been accepted worldwide for a decade now. Diabetics have therefore been automatically assigned to the high risk category.

This view is now questioned by a meta-analysis by Bulugahapitiya et al.[53] Their meta-analysis did not support the hypothesis that diabetes is a 'coronary heart disease equivalent. A meta-analysis of 45,108 patients showed that patients with diabetes without prior myocardial infarction had a 43% lower risk of developing total coronary artery disease events compared with patients without diabetes with previous myocardial infarction (summary odds ratio 0.56, 95% confidence interval 0.53-0.60). The explanation for this discrepancy is likely to be that diabetic patients now receive optimal aggressive treatment strategy including, the use of statins and antihypertensive agents.

Public health decisions to initiate additional investigations to screen for coronary artery disease in patients with diabetes should therefore now be based on appropriate patients' coronary artery disease risk estimates rather than a 'blanket' "routine" investigations approach.

3.3 Stratification for cardiovascular disease risk

From the global cardiovascular assessment, asymptomatic individuals can be categorised as low risk (<10% 10-year risk of coronary artery disease), intermediate risk, and high risk (more than 20% 10 year risk of coronary artery disease). Further testing for coronary artery diseaseto reclassify asymptomatic individuals in the intermediate risk group to high risk group need to be considered because interventions to reduce cardiovascular risk is intensified as the risk category increases from low to high risk individuals.

Low risk asymptomatic individuals

C In low risk individuals (<10% 10-year risk of coronary artery disease) further testing for coronary artery disease is not routinely recommended.[55]

Grade C, Level 2++

In adults with low risk for coronary artery disease events, the United States Preventive Task Force recommends against routine further screening with resting ECG, exercise treadmill test, or electron-beam computerised tomography scanning to obtain the coronary artery calcium score.[55]

Intermediate and high risk asymptomatic individuals

C There is insufficient evidence to recommend for or against routine screening for coronary artery disease in asymptomatic individuals with intermediate (10-20% 10-year risk of coronary artery disease) or high risk (>20% 10-year risk of coronary artery disease). Given the lack of evidence, in intermediate and high risk asymptomatic individuals, further screening should be limited to the following selected situations[55]:

- The exercise treadmill test (exercise treadmill testing) may be performed to: evaluate those with multiple risk factors as a guide to risk-reduction therapy; evaluate asymptomatic men older than 45 years of age and women older than 55 years of age who plan to start vigorous exercise, are involved in occupations in which impairment might impact public safety or are at high risk for coronary artery disease because of other diseases; or to evaluate asymptomatic persons with diabetes who plan to start vigorous exercise.

- The coronary calcium score (CACS) on electron-beam computed tomography may be used in the intermediate coronary artery disease risk patient to decide if the patient should be reclassified to a higher risk status based on a high CACS.

Grace C, Level 2++

3.4 Cardiovascular screening tests selectively indicated

3.4.1 Resting Electrocardiography (ECG)

B The routine use of resting ECG for screening for coronary artery disease in asymptomatic individuals is not recommended.[56-60]

Grade B, Level 2++

Presently there is no evidence that the routine ambulatory ECG provides reliable information concerning ischemia in asymptomatic subjects who do not have known coronary artery disease.[56, 58] The 2002 ACC/AHA guidelines also recommends against use of a routine ECG to screen asymptomatic patients.[59] One study showed that approximately

30% of patients who have angiographically proven coronary artery disease have a normal resting ECG.[60]

The prevalence of the most common ECG abnormalities (Q waves, left ventricular hypertrophy, bundle-branch blocks, and ST-segment depression) ranges from 1% to 10%. Because of the limited sensitivity of resting ECG and the low prevalence of coronary artery disease in asymptomatic adults, a majority of coronary artery disease events will occur among those with an initially normal ECG (that is, those who test false negative). In low-risk asymptomatic populations, most positive ECG test results occur in those who will not have a coronary artery disease event in the next 5 to 10 year.[55]

A local study of asymptomatic patients referred to a tertiary cardiac centre for the suspicion of coronary artery disease (coronary artery disease) based solely on ECG findings found a prevalence of 0.8% CAD in this population, suggesting that using the ECG as a screen for coronary artery disease is not helpful.[61]

In symptomatic patients however, the resting 12-lead ECG provides valuable information about myocardial ischemia in those who have known coronary artery disease, and may assist in the evaluation of atypical chest pain.

3.4.2 Exercise treadmill testing

B Routine use of the exercise treadmill testing to screen for coronary artery disease in asymptomatic low-to-moderate risk individuals is not recommended. Its use among those in the highest risk group (10-year predicted coronary artery diseaserisk of 20%) may be considered.[62-64]

Grade B, Level 2++

No study has directly examined the effect on coronary artery disease outcomes following screening of asymptomatic patients with exercise treadmill testing. Although exercise tolerance testing correctly identifies severe coronary artery obstruction in up to 2.7% of those screened, most positive findings will be false when the risk of coronary events is low.[62] In one meta-analysis, the sensitivity of exercise treadmill testing ranged from 23% to 100%, and the specificity ranged from 17% to 100%.[63]

The prevalence of an abnormal exercise treadmill testing (ST-segment depression > 1 mm) reportedly ranges from 5% to 25%. The yield of exercise treadmill testing in detecting severe coronary artery disease in asymptomatic middle-aged men is estimated to be 0.5%. The positive predictive value for future coronary artery disease in recent cohort studies (most of them conducted with asymptomatic men) is low (range, 6% to 48%).[55]

One study reported that 71% of those without symptoms who had an abnormal exercise treadmill testing had no angiographically demonstrable coronary artery disease.[65] The exercise treadmill testing can be normal or nondiagnostic in a large proportion of patients who will go on to have a coronary artery disease event, which may be explained partly by the fact that many acute coronary artery disease events result from sudden occlusion of a previously unobstructed artery segment.[66]

However, four contemporary screening studies (from the Cooper Clinic, the Framingham Heart Study and two studies from Norway) have demonstrated impressive incremental risk ratios for the synergistic combination of the standard exercise test and risk factors. [64, 67-70]

In a report from the Framingham Heart Study exercise treadmill testing provided additional prognostic information in age- and Framingham Risk Score-adjusted models, particularly among those in the highest risk group (10-year predicted coronary artery disease risk of 20%).[64]

3.4.3 Cardiac stress imaging

D Cardiac stress imaging is not recommended for routine screening for coronary artery disease in asymptomatic patients at low risk.[59]

Grade D, Level 4

The use of cardiac stress imaging in the asymptomatic person is generally reserved for patients who have abnormal exercise ECG. The ACC/AHA 2002 guideline on stable angina recommended that asymptomatic patients with a low-risk exercise treadmill score should not have stress imaging performed.[59]

D Cardiac stress imaging or stress echocardiography may be considered in a patient who has moderate to high risk of coronary artery disease and abnormal exercise ECG.[59, 71]

Grade D, Level 4

A patient who has a moderate to high risk of coronary artery disease and abnormal exercise ECG may benefit from further testing with exercise myocardial perfusion imaging or stress echocardiography.59 In a study of patients evaluated for the presence of coronary artery disease, stress echocardiography had better prognostic capabilities than stress electrocardiography.[71]

Although myocardial perfusion imaging has clearly been shown to provide powerful prognostic information in a wide range of patient subgroups, including diabetics, it does not follow that testing will reduce events.

For example, the incremental diagnostic and prognostic value of myocardial perfusion imaging in diabetics is well established. Diabetics have a high risk of coronary artery diseaseand death from coronary artery disease. One might conclude that diabetics should undergo screening to detect silent coronary artery diseaseespecially since diabetics may have minimal or no symptoms from ischemia due to autonomic neuropathy. However, a recently published randomised trial, namely, the DIAD (Detection of Ischemia in Asymptomatic Diabetes) study did not find evidence to support screening.

The DIAD study assessed the value of myocardial perfusion imaging for screening of asymptomatic diabetic patients with normal resting ECGs, by randomising over 1,000 such patients to routine nuclear perfusion imaging versus standard care, and following up the patients to assess the possible long term benefits of early detection of coronary artery disease. Approximately 22% of the screening group were found to have evidence of myocardial ischemia, and 6% were found to have high-risk findings. Nevertheless, at the end of 4.8 years, there was no difference in outcomes between the two groups. The authors concluded that there were no grounds to advocate screening using myocardial perfusion imaging even in a relatively high-risk group such as diabetics.[48]

Possible reasons for the lack of a benefit from screening is that medical therapy for both groups (e.g. lipid lowering) reduces event rates, and was probably optimal, regardless of the scan findings, whereas revascularisation (which might be the expected benefit of discovering coronary artery diseaseearlier) has not yet been shown to prevent events in asymptomatic patients. In addition, many of the standard care patients also underwent myocardial perfusion imaging during the study period, (although this may have been due to development of symptoms).

The conclusions of the study read: "In the light of our findings, routine screening for inducible ischemia in asymptomatic patients with type 2 diabetes cannot be advocated for 4 reasons. First, the yield of detecting significant inducible ischemia is relatively low. Second, the overall cardiac event rate is low. Indeed, even our participants with moderate or large defects and the highest event rate would be conventionally assigned to an intermediate risk category. Third, routine screening does not appear to affect overall outcome. Finally, routine screening of millions of asymptomatic diabetic patients would be prohibitively expensive."

D Stress imaging is not useful for patients with no clinical risk factors who are undergoing intermediate-risk non-cardiac surgery. Such testing is also not useful for asymptomatic patients undergoing low-risk non-cardiac surgery.[49]

Grade D, Level 4

Pre-operative testing with cardiac stress imaging is a form of screening since it may be utilised in asymptomatic individuals with no prior history of heart disease. The idea of "clearing" patients for non-cardiac surgery is intuitively attractive but the reality is routine testing is not useful. A randomised trial of routine testing versus standard care did not show any reduction in event rates for patients with intermediate risk of events (DECREASE II). The CARP study, in which patients with ischaemic heart disease due for non-cardiac surgery were randomised to revascularisation prior to surgery or standard care, showed no benefit to prophylactic revascularisation. In addition, a pilot study randomising patients with high-risk evidence of ischaemia to revascularisation versus no revascularisation showed no benefit. (DECREASE V). Stress imaging is therefore not recommended for the following categories of asymptomatic patients: (a) patients with no

clinical risk factors undergoing intermediate-risk non cardiac surgery, and (b) patients undergoing low-risk non cardiac surgery.[49]

D Cardiac stress imaging may be considered as pre-operative screening in asymptomatic individuals prior to non-cardiac surgery whose: (a) functional status is poor (less than 4 Mets) or unknown, (b) undergoing vascular surgery or intermediate risk surgery (intra-peritoneal and intra-thoracic surgery, carotid endarterectomy, head and neck surgery, orthopaedic surgery, prostate surgery) with (c) 1 or more risk factors (history of heart disease, history of compensated or prior heart failure, history of cerebrovascular disease, diabetes mellitus, or renal insufficiency) and (d) in whom the results of testing will change management.[72-74]

Grade D, Level 4

3.4.4 Coronary artery calcium score (CACS)

D The use of coronary artery calcium score (CACS) by means of computerised tomography may be considered in selected situations, namely:[75]

(a) asymptomatic patients with intermediate coronary artery disease risk (between 10% and 20% 10-year risk of estimated coronary events, based on the possibility that such patients might be reclassified to a higher risk status based on high CACS, and subsequent patient management may be modified,

(b) patients who have atypical cardiac symptoms but otherwise considered to be at low risk of coronary disease, who may benefit from CACS to help in ruling out the presence of obstructive coronary disease.

Grade D, Level 4

Electron beam computer tomography (EBCT) assesses atherosclerosis by measuring the extent of vascular calcification or Coronary Artery Calcium Score (CACS). In a meta-analysis of highly selected, symptomatic groups of patients, EBCT had a pooled sensitivity of 90.5% and specificity of 49.2%.

Similar data for those who have no symptoms are lacking. One study demonstrated that EBCT predicted silent ischemia as demonstrated by abnormal single photon emission computed tomography (SPECT) scan in asymptomatic moderate-to-high risk patients. Increased coronary artery calcium scores predict subsequent development of heart disease events in the following 3.5 years in asymptomatic patients, though the increase is not directly proportional to scores.

In a cost-effectiveness analysis of EBCT, the marginal cost of using EBCT to identify an additional patient "at risk" that had been missed by the Framingham Risk Index is US$9789. The study found that the cost per quality-adjusted life year saved was US$86,752 when used to screen a population considered to be at low risk for coronary artery disease.

For patients with symptoms of coronary artery disease, EBCT has a sensitivity of 80% and a specificity of 40% for detecting angiographically demonstrated coronary artery disease. Similar data for those who have no symptoms are lacking.

A report from the MESA (Multi-Ethnic Study of Atherosclerosis) cohort found a strong association between coronary calcification and coronary artery disease risk with an adjusted relative hazard for coronary events between 3.6 and 9.7, depending on the amount of calcification The c-index (discriminant accuracy) for risk factors plus calcium score was excellent at 0.83 for MI and death, and 0.82 for all coronary artery disease events ($p<0.01$ in comparison with risk factors, 0.79 and 0.77, respectively).[76]

The ACCF/AHA Expert Consensus Document on Coronary Artery Calcium AFFC/AHA Scoring judged that it may be reasonable to consider use of CACS measurement in asymptomatic patients with intermediate coronary artery disease risk (between 10% and 20% 10-year risk of estimated coronary events) based on available evidence that demonstrates incremental risk prediction information in this selected (intermediate risk) patient group. This conclusion is based on the possibility that such patients might be reclassified to a higher risk status based on high CACS, and subsequent patient management may be modified in patients with low coronary artery disease risk. The same expert document does not recommend use of coronary artery calcium measurement in low coronary artery disease risk (below 10% 10-year risk of estimated coronary artery disease events).[75]

In asymptomatic patients with high coronary artery disease risk (greater than 20% estimated 10-year risk of estimated coronary artery disease events, or established coronary disease, or other high-risk diagnoses) the expert document does not advise coronart artery calcium measurement as such patients are already judged to be candidates for intensive risk reducing therapies based on current guidelines.

Patients referred for calcium scoring should be informed of the small theoretical risks of malignancy as a result of radiation exposure. One study estimated that a single screening at the age of 40 years was estimated to result in a lifetime excess cancer risk of 9 (range, 3-42) and 28 (range, 9-130) cancers per 100 000 persons for men and women, respectively, based on a median dose of 2.3 mSv (range, 0.8-10.5 mSv) reported in a survey.[77] Similar remarks on radiation risks apply to myocardial perfusion imaging studies as well.[78]

3.4.5 CT coronary angiography

D Use of CT coronary angiography as a screening test in low- and intermediate- risk asymptomatic persons is not recommended.[79]

Grade D, Level 4

Use of CT coronary angiography as a screening test in low- and intermediate-risk asymptomatic persons is not recommended and its value as a screening test in high-risk asymptomatic persons is also uncertain.

CT coronary angiography is accurate for excluding coronary artery disease, and has been considered as a potential screening test for coronary artery disease. Concerns over radiation exposure have been raised, with an estimated risk of additional lifetime cancer of about 1 in 1007 for a 40 year old man.[80] This risk may appear small, but in a screening situation, the benefit of screening may be similar i.e. 1 in a 1000. However, recent technical developments have allowed for lower radiation doses.

Another concern is the detection of incidental findings such as pulmonary nodules, which might lead to further serial scanning to exclude malignancy In one study, 22% of scans had significant non-cardiac findings.[81] A local study had similar findings (19% significant non-cardiac findings).[82]

A recent study described the results of screening for coronary artery disease in 1,000 asymptomatic Koreans using CT angiography Atherosclerotic plaques were identified in 22% of individuals and 4% had only non-calcified plaques. 52 (5%) subjects had significant (>50%) diameter stenosis and 21 (2%) had severe (>75%) stenosis. In the 215 patients with evidence of coronary artery disease, there were no cardiac deaths, and 15 events, of which 14 were due to revascularization, and 1 was due to unstable angina.[83] Based on this study, which had no control arm, it is difficult to conclude that screening would be helpful.

A recent American Heart Association scientific statement (2008) on the role of non-invasive coronary artery imaging does not support using CT angiography, and classifies its use as inappropriate.[79] To quote from this statement"Neither CT coronary angiography nor MRA should be used to screen for coronary artery disease in patients who have no signs or symptoms suggestive of coronary artery disease."

The ACCF/ ACR/ SCCT/ SCMR/ ASNC/ NASCI/ SCAI/ SIR Appropriateness Criteria for Cardiac Computed Tomography and Cardiac Magnetic Resonance Imaging84 published in 2006 based on expert consensus, rated the use of CT coronary angiography in asymptomatic patients as: "inappropriate" for patients with a low pretest likelihood of disease,; "inappropriate" for patients with an intermediate likelihood of disease; and "uncertain" for patients with a high likelihood of disease.

Coronary angiography can be used to establish the diagnosis of coronary artery disease, and may be appropriately used to evaluate patients who have typical anginal symptoms. However, of all patients undergoing outpatient coronary angiography, an estimated 0.08% will die as a result of the procedure and 1.8% will experience a potentially serious complication.[85]

3.4.6 Carotid intima-media thickness

C Carotid intima-media thickness measurement is not recommended for routine cardiovascular disease screening.[12, 86]

Grade C, Level 2+

Carotid intima-media thickness refers to the combined thickness of the tunica intima and tunica media layers of the carotid arteries. This is

usually measured by high-resolution B-mode ultrasound. The range of carotid intima-media thickness in the general Singapore population has not been established. In a large community-based study in the United States, the median carotid intima-media thickness was between 0.5 and 1mm; fewer than 5% had carotid intima-media thickness more than 2 mm.[87]

Several studies have noted a moderate association between carotid intima-media thickness and the presence of coronary atherosclerosis and risk of future cardiovascular events.[88-89]

The hazard ratio for the vascular end-points (coronary artery disease stroke and vascular death) increases 1.3 times for each standard deviation increment in maximum carotid intima-media thickness in a large multiethnic cohort.[76] The risk may be even higher in younger (<45 years old) compared to older adults.[88] The risk of MI or stroke is almost 4 times in the quintile of the highest thickness compared to the lowest thickness among the elderly[90]; per standard deviation of carotid intima-media thickness increase, the risk was each about 1.5 times.[91] The risk of coronary artery disease may be more than 3 times higher in middle-aged women compared to men when carotid intima-media thickness was 1 mm or more.[92] Among Asians, increased carotid intima-media thickness raised stroke risk among elderly Japanese men[93] and all-cause and cardiovascular mortality.[94] However, much of the excess risk is attenuated when adjusted for traditional risk factors.

Due to concerns about the accuracy of carotid intima-media thickness measurement in non-research settings, considerable inter-observer variability, differences of methods of carotid intima-media thickness measurement and interpretation and limited availability at select centers, as well as uncertainty of the effects of carotid intima-media thickness independent of LDL-cholesterol, the routine use of carotid intima-media thickness measurement to improve clinical decision of a cardiovascular risk score cannot be recommended in this present state of the knowledge.[12, 86]

The use of a statin among middle-aged adult with raised LDL-cholesterol and moderate carotid intima-media thickness thickening statistically reduced the rate of intima-media thickness progression; however, the clinical significance of this reduction remains to be seen.[95]

3.4.7 Ankle-brachial index

The ankle brachial index is a test for peripheral vascular disease. It is determined by measuring systolic blood pressure at the ankle, based on palpation or ultrasonographic measurement of the dorsalis pedis pulse, and dividing this by the systolic blood pressure measured in the arm.[12]

Peripheral Vascular Disease

D It is recommended that the ankle brachial index be considered as a screening test for individuals with high risk for peripheral vascular disease, namely[96]

(a) Age less than 50 years, with diabetes and one other atherosclerosis risk factor (smoking, dyslipidemia, or hypertension).
(b) Age 50-69 years and history of smoking or diabetes.
(c) Age 70 years and older.

Grade D, Level 4

Cardiovascular disease

B The ankle brachial index may be considered for purpose of reclassification of an individual who has intermediate risk of coronary artery disease.[97]

Grade B, Level 2+

The ankle brachial index has also been shown to be associated with coronary artery disease. The attraction of ankle brachial index screening as a biomarker of cardiovascular risk is that this test is relatively easy to do in the primary care setting and is non-invasive.

A systematic review of the literature from 1996 by the United States Preventive Task Force on the use of the ankle brachial index to screen asymptomatic men and women with no history of coronary artery disease to prevent coronary artery disease events concluded that current evidence available then was insufficient to provide a recommendation because not all the cases selected were asymptomatic.[12]

Despite the potential value of ankle brachial index for identifying at risk patients for intervention, a recent randomised trial on the use of aspirin[98] in individuals with abnormal ankle brachial index did not support screening. The results of the study showed that among participants without clinical cardiovascular disease in a general population, identified with a low ankle brachial index aspirin did not reduce risk for vascular events or all-cause mortality. The trial was stopped early because of the improbability of finding benefit and a trend for increased risk for major haemorrhage in the aspirin group. Groups did not differ for vascular events, all-cause mortality, or major haemorrhage. Comments on this trial pointed out that the study was inadequately powered (type II error).[99]

4 Biochemical tests in cardiovascular screening

4.1 Lipid screening

GPP For lipid screening, it is recommended that testing be carried out on a venous sample sent for laboratory analysis and not from a finger-prick capillary sample tested on a physician office or bedside testing device.

GPP

Significant misclassifications can occur with the use of capillary cholesterol as a predictor of CV risk. Hence, testing for lipid screening should be carried out from a venous sample for laboratory analysis.

Blood should be drawn from subjects who have not had any acute inter-current illness for three weeks, and on their usual diet for at least one week before testing. Lipid levels are non-indicative of baseline state in severe psychological stress between 24 hours and up to three months after a major medical event such as an acute myocardial infarction.

B For lipid screening, it is recommended that a fasting venous sample should be collected for lipid levels of total cholesterol, triglycerides, high density lipoprotein cholesterol (HDL-C). The low density lipoprotein cholesterol (LDL-C) can be reported as a calculated value or as a directly measured result.[100]

Grade B, Level 2++

The fasting sample for lipid levels of total cholesterol, triglycerides, high density lipoprotein cholesterol (HDL-C), and low density lipoprotein cholesterol (LDL-C) constitutes the basic lipid profile or panel.

The LDL-C level is calculated by the Friedewald formula:
LDL-C = Total cholesterol – [HDL-C + (Triglyceride/2.2)] with all units in (mmol/L)

The Friedewald formula is invalid when Triglyceride is >4.5 mmol/L. In such instances, a measured LDL-C is a valid and acceptable alternative.

Laboratories do continue to report lipid profile in imperial units of milligram per deciliter (mg/dl) and the conversion factor is:
To convert total cholesterol, HDL-C, and LDL-C from mmol/L to mg/dl, multiply by the factor 38.6.
To convert triglyceride from mmol/L to mg/dl, multiply by the factor 88.5.

Total cholesterol and HDL-C determinations can be carried out at any time of day and in the non-fasting state. Triglyceride levels should be obtained only following 10-12 hours of fasting.

There are a number of new candidate biomarkers proposed as risk factors and predictors of cardiovascular disease. These biomarkers are termed "emerging risk factors" but their roles in cardiovascular disease is not as well documented as dyslipidemia, high blood pressure, and smoking – the traditional major risk factors. Evidence is evolving for these respective makers, but as a rule these markers are generally not recommended for routine cardiovascular disease screening.[12]

4.2 Lipoprotein (a), Apolipoproteins A1 and B

B Lipoprotein(a) determination is not recommended for routine cardiovascular screening.[101]

Grade B, Level 2++

The reported higher cardiovascular risk among South Asians is partly explained by an increased prevalence of abdominal obesity, glucose intolerance, hyper-triglyceridemia, low HDL-C levels and elevated levels of lipoprotein(a).[101]

Each of the atherogenic lipoprotein particles - very low density lipoprotein cholesterol (VLDL), intermediate-density lipoprotein cholesterol (IDL), LDL and lipoprotein(a) contains one molecule each of apolipoprotein B. Serum concentration of apolipoprotein B reflects the total number of these particles.

Prospective studies have found apolipoprotein B to be a better estimate of the risk of vascular events than LDL-C. Risk is highest in individuals with apolipoprotein B levels higher than 1.2g/L and triglyceride levels higher than 1.5 mmol/L. This profile is often associated with the presence of smaller, denser LDL particles, which are more atherogenic and prevalent in patients with the metabolic syndrome and type 2

diabetes. Apolipoprotein A is associated with HDL particles. There is no requirement for a fasting specimen for apolipoprotein measurement.

C Further to a global cardiovascular risk assessment, lipoprotein(a) measurements may be useful in individuals with a strong family history of premature cardiovascular disease.[102]

Grade C, Level 2+

Lipoprotein(a) is an LDL particle in which apolipoprotein B is attached to the apolipoprotein A protein. Apolipoprotein A has structural homology to plasminogen, and competitive binding can impair fibrinolysis. Lipoprotein (a) has been identified as an independent risk factor for coronary artery disease.

Lipoprotein (a) determination is not recommended for routine cardiovascular disease screening. Lipoprotein subclasses, especially the number or concentration of small dense LDL particles, have been shown to be related to the development of initial coronary artery disease events, but data are not adequate to show added benefit over standard risk assessment for primary prevention.[102]

D Routine apolipoprotein B determination is not recommended.[103]

Grade D, Level 4

Although apolipoprotein B measures atherogenic lipoproteins and is a good predictor of cardiovascular disease risk (equal or better to LDL-C), it is only a marginally better predictor than the current lipid profile and should not be routinely measured at this time for use in global risk assessment. There are technical issues of reliability and comparability of apolipoprotein B and apolipoprotein A1 assays.[103]

4.3 Inflammation biomarkers

4.3.1 High sensitivity C-reactive protein

C It is recommended that caution be exercised in application of high sensitivity C-reactive protein as a screening test as risk prediction is not established in Asians and in the elderly.[104]

Grade C, Level 2+

C-Reactive Protein (CRP) does not appear to be directly atherogenic. When measured using a high sensitivity assay, high sensitivity CRP is a marker of inflammation, and may potentially identify asymptomatic individuals at risk for acute coronary events. The incremental value of high sensitivity CRP testing for risk assessment in clinical practice remains debatable.[104]

B The measurement of high sensitivity C-reactive protein is recommended only if the 10-year predicted risk based on standard global risk assessment is 5% or more.[105-109]

Grade B, Level 2+

The decision to measure high sensitivity CRP depends on the results of a standard global risk assessment:

- If the 10-year predicted risk is <5%, high sensitivity CRP should not be measured.[110]
- If the 10-year risk is 5% to <10%, a higher re-classification may be influenced with the test. More information is needed on clinical application, particularly in relation to longer-term lifetime risk prediction and selection of an appropriate intervention (lifestyle/ medical).[105]
- If risk is intermediate (10-20%) and uncertainty remains as to the use of preventive therapies such as statins or aspirin, then high sensitivity CRP measurement might be useful for further stratification into a higher or lower risk category.[106-107]

High sensitivity CRP using standardized assays categorizes patients as follows: (a) Low risk <1.0 mg/L; (b) Average risk 1.0-3.0 mg/L; (c) High risk >3.0 mg/L; (d) Very high risk 10.0 mg/L.[110]

GPP If the high sensitivity CRP concentration is <3 mg/L, it does not need to be repeated. If the value is >3 mg/L, repeat the measurement at least 2 weeks later with patient in stable state, free of infection or acute illness. Select the lower of the 2 results as the patient's value.

GPP

4.3.2 Homocysteine

GPP Plasma homocysteine measurement is not recommended in cardiovascular screening.

GPP

Elevated plasma homocysteine is a predictor of adverse outcomes in patients with coronary artery disease, and is prevalent in patients with renal impairment or peripheral vascular disease. The benefit of treating coronary artery disease patients with folic acid and vitamin B12 supplements has not been established. Plasma homocysteine measurement is not recommended.

4.3.3 Fibrinogen

B Fibrinogen measurement is not recommended for cardiovascular disease screening.[111]

Grade B, Level 2++

Although data indicates that fibrinogen is an independent marker of cardiovascular disease risk, there are significant analytical concerns and uncertainty in identifying treatment strategies.

4.4 Natriuretic peptides (BNP and NT-proBNP)

B Natriuretic peptides (BNP and NT-proBNP) measurement is not recommended for cardiovascular disease screening.[112]

Grade B, Level 2++

Although elevated BNP or NT-proBNP concentrations are associated with increased mortality in the subsequent years, the benefits of therapy based on these measurements are uncertain.

5 Screening for asymptomatic cardiovascular disease in diabetes mellitus and chronic renal disease

5.1 Screening for cardiovascular risk factors in diabetes mellitus

Type 2 diabetes mellitus has been identified as a major risk factor for atherosclerotic disease. In Singapore, almost 60% of subjects with diabetes mellitus die as a consequence of cardiovascular disease.[113-114] The case-fatality is also higher in subjects with type 2 diabetes mellitus. As many as 50% of persons suffering their first myocardial infarction die, and never become eligible for measures intended for secondary prevention. Primary prevention of cardiovascular disease is a major goal of therapy in type 2 diabetes mellitus. Apart from hyperglycaemia, persons with type 2 diabetes mellitus often have several other abnormalities including hypertension, dyslipidaemia, and obesity.

5.1.1 Global cardiovascular assessment

D Global cardiovascular assessment is recommended for all patients with diabetes mellitus.[114]

Grade D, Level 4

Although not all studies have been in concordance, diabetes mellitus has sometimes been regarded as a coronary risk equivalent.[53-54] (Also see Sections 3.2 & 3.3 page 25 and 27). There is evidence however that even amongst people with diabetes, individuals may have varying propensity to develop incident cardiovascular disease.[115] Hence identifying the varying cardiovascular risk factor burden and intensive (individual) risk factor modification is an integral part of the management of the patient with type 2 diabetes. Hence, a global cardiovascular assessment is recommended for all patients with diabetes mellitus.[114]

5.1.2 Medical history, physical examination, blood pressure, laboratory tests, and ECG

D It is recommended that the assessment of cardiovascular risk in persons with type 2 diabetes mellitus include a medical history, physical examination, blood pressure, fasting serum lipids, assessment of urine for microalbuminuria or proteinuria, and a resting ECG at baseline.[114]

Grade D, Level 4

Atherosclerosis in type 2 diabetes mellitus is multifactorial in nature. The assessment of cardiovascular risk in persons with type 2 diabetes mellitus should include: [114]

History-- which should include:
- Smoking
- Hypertension
- Pre-existing cardiovascular disease (including angina, myocardial infarction, stroke, PAD)
- Family history of premature coronary artery disease (non-modifiable)

Physical examination -- which should include:
- Assessment for peripheral vascular disease
- Measurement of blood pressure at every visit

Tests -- which should include:
- Fasting serum lipids at or soon after diagnosis and at least annually
- Urine microalbumin or protein at least annually
- Electrocardiogram (resting) routinely at baseline. Subsequent ECG may be performed when clinically indicated.

Where identified risk factors are modifiable, appropriate risk factor modification should be discussed with the patient. Besides pharmacological therapy, due emphasis should be paid to discussion of lifestyle factors.

There is epidemiological evidence that amongst people with no known prior coronary artery disease, those with diabetes have higher rates of sudden cardiac death when compared to those without diabetes.[116]

This, together with the notion that diabetes is a cardiovascular risk equivalent, at least in some, suggests that a significant number of people with diabetes may have silent prevalent coronary artery disease In the DIAD study, approximately 22% of subjects who were asymptomatic of cardiovascular disease, were found to have evidence of myocardial ischemia using myocardial perfusion imaging at baseline screening. However, at the end of 4.8 years, there was no difference in outcomes between those who were screened when compared to those who were not screened.[48] The authors concluded that there were no grounds to advocate screening using myocardial perfusion imaging even in a relatively high-risk group such as people with diabetes (Also see Section 3.4.3 pg 30).

5.1.3 Evaluation of people with diabetes mellitus prior to exercise

D For asymptomatic individuals with diabetes above 40 years of age and intending to engage in more than low intensity exercise, a pre-exercise evaluation and a graded exercise stress ECG are recommended.[114]

Grade D, Level 4

For asymptomatic patients with diabetes above 40 years of age and intending to engage in more than low intensity exercise, a pre-exercise evaluation and a graded exercise stress ECG are recommended.[114] This helps to refine exercise prescription so that a level of intensity of exercise customized to the patient's risk and fitness can be selected and discussed with the patient.[117] The pre-exercise evaluation should include a full medical history and examination to identify macrovascular, microvascular and neurological complications.

For asymptomatic people with diabetes who are intending to engage in low intensity exercise, a stress test should not be necessary in the absence of high risk clinical or (resting) ECG features.[117]

5.2 Screening for cardiovascular risk factors in chronic kidney disease

5.2.1 Screening for cardiovascular disease and risk factors

D In patients at risk of chronic kidney disease, screening for risk factors for cardiovascular disease and for coronary artery disease is recommended at baseline and when patients become symptomatic of renal disease.[118]

Grade D, Level 4

Traditional cardiovascular risk factors, including advanced age, diabetes mellitus, hypertension and dyslipidemia, have an important role in the progression of cardiovascular disease in patients who have a reduced glomerular rate, especially in those with mild-to-moderate kidney disease.[118]

Increased awareness of concomitant cardiovascular disease (cardiovascular disease) in all chronic kidney disease patients is necessary. chronic kidney disease is known to be associated with increased cardiovascular disease incidence and prevalence. cardiovascular disease, broadly divided into congestive heart failure, ischaemic heart disease and/or left ventricular hypertrophy, has an estimated overall prevalence of 8 – 40% of patients with chronic kidney disease.[119] Hypertension, a risk factor for coronary artery disease and left ventricular hypertrophy, occurs in 87 – 90% of all chronic kidney disease patients. Prevalence of left ventricular hypertrophy has also been shown to rise at each stage of chronic kidney disease, reaching 75% at the time of dialysis initiation.[118]

5.2.2 Screening for severity of chronic kidney disease to determine the cardiovascular disease burden

D Since the single most important determinant of cardiovascular disease burden is the severity of chronic kidney disease, screening for the presence and level of renal impairment is recommended.[120]

Grade D, Level 4

The severity of chronic kidney disease is the single most important determinant of cardiovascular disease burden.[118] Moderate (creatinine clearance30 – 59 ml/min) to severe (creatinine clearance< 30 ml/min) renal insufficiency are risk factors for atherothrombotic vascular events and cardiovascular mortality.[120] When compared with subjects with essential hypertension and normal kidney function, chronic kidney disease patients had more severe left ventricular hypertrophy across the chronic kidney disease continuum (stage 2 to 5).[121] A retrospective Korean study of 3,637 patients showed rising incidence of coronary artery disease with increasingly severe chronic kidney disease stage: 48% coronary artery disease incidence in chronic kidney disease stage 1 rising to 81% in stage 5.[122]

In the majority of patients, chronic kidney disease can be detected with 2 simple tests: a urine test for the detection of proteinuria and a blood test to estimate the glomerular filtration rate.These two tests facilitate detection of chronic kidney disease by all physicians by allowing for identification of chronic kidney disease without first requiring determination of its cause.[123]

Given that chronic kidney disease per se is a risk factor for cardiovascular disease, retarding the progression of chronic kidney disease through the control of hypertension and the use of angiotensin-receptor blockeris vital and should complement traditional ways of reducing the cardiovascular disease burden in this subpopulation such as optimizing the treatment of dyslipidemia and diabetes mellitus.[124-125]

Although cardiovascular disease has been shown to be prevalent in chronic kidney disease, screening and treating hyperlipidaemia, have not resulted in positive patient outcomes. The AURORA study of 2,776 patients undergoing haemodialysis failed to show a significant decline in cardiovascular mortality in the rosuvastatin-treated arm compared to the placebo-controlled group, despite lowering LDL-cholesterol.[126]

A similar study of diabetics on maintenance haemodialysis randomized to receive either atorvastatin or placebo, showed no significant reduction in both cardiovascular and cerebrovascular mortality in the statin-treated group, despite highly significant reduction in LDL-cholesterol.[127] Note however that a paper presented by the authors of the Study of Heart and Renal Protection (SHARP) recently at the American Society of

Nephrology Renal Week 2010 showed that cholesterol lowering with a combination of simvastatin and ezetimibe in patients with kidney disease significantly reduced the risk of "major atherosclerotic events" by 17% and the primary end point for the study, major vascular events, by almost the same degree. The results have not yet been published.

6 Screening for abdominal aortic aneurysm, peripheral arterial disease, cerebrovascular disease and atrial fibrillation

6.1 Abdominal aortic aneurysm

B Routine ultrasonographic screening of men 65 years and older for abdominal aortic aneurysm may be considered, particularly in those who have ever smoked (current and former smokers).[128-131]

Grade B, Level 2++

The United States Preventive Services Task Force found good evidence that screening for abdominal aortic aneurysm and surgical repair of large abdominal aortic aneurysms (5.5 cm or more) in men aged 65 to 75 who have ever smoked (current and former smokers) leads to decreased abdominal aortic aneurysm-specific mortality. There is good evidence that abdominal ultrasonography, performed in a setting with adequate quality assurance (i.e., in an accredited facility with credentialed technologists), is an accurate screening test for abdominal aortic aneurysm. There is also good evidence of important harms of screening and early treatment, including an increased number of surgeries with associated clinically-significant morbidity and mortality, and short-term psychological harms. Based on the moderate magnitude of net benefit, the United States Preventive Services Task Force concluded that the benefits of screening for abdominal aortic aneurysm in men aged 65 to 75 who have ever smoked outweigh the harms.[128-129, 132-133]

B Routine screening for abdominal aortic aneurysm in women is not recommended.[134]

Grade B, Level 2+

A randomized controlled trial in UK assessed the effects of screening women for abdominal aortic aneurysm.[134] Some 9342 women aged 65-80 years were entered into the trial and randomized to age-matched screen and control groups. A single ultrasonographic scan was offered to women in the screening arm of the study. Women with an abdominal aortic aneurysm received follow-up scans, and were considered for elective surgery if certain criteria were met. The prevalence of abdominal aortic aneurysm was six times lower in women (1.3 per cent)

than in men (7.6 per cent). Over 5- and 10-year follow-up intervals, the incidence of rupture was the same in the screened and control groups of women. The conclusion was screening women for abdominal aortic aneurysm was neither clinically indicated nor economically viable.

6.2 Peripheral vascular disease

See under Ankle brachial index page 37-38.

6.3 Carotid artery stenosis

D Routine screening for carotid artery stenosis is not recommended.[135-138]

Grade D, Level 4

The prevalence of asymptomatic carotid stenosis in the general population in Singapore is not known. In Western populations, between 5% and 10% of men and women >65 years of age have carotid stenoses >50%, with 1% having stenoses >80%.[139-141] The annual stroke risk among persons with an asymptomatic carotid artery stenosis between 50% and 99% is between 1% and 3.4%.[142-148] Two of 4 clinical trials have shown the benefit of endarterterectomy in reducing the risk of stroke.[149-152] However, the benefit of endarterectomy depends highly on surgical risk, and the benefit can be negated by peri-procedural complications. Although highly selected patients may benefit, in view of its low prevalence and small benefit, screening of general populations for asymptomatic carotid stenosis is unlikely to be cost-effective.[135-137]

The United States Preventive Services Task Force also recommends against screening for carotid stenosis in the general population.[138] In the general population, screening with carotid with duplex ultrasonography would result in many false-positive results. This would lead either to surgeries which are not indicated or to confirmatory angiography. As the result of these procedures, some people would have serious harm (death, stroke, and myocardial infarction) that outweigh the potential benefit that surgical treatment may have in preventing stroke. The major risk factors for carotid artery stenosis are older age, male sex, hypertension, smoking, hyperlipidemia, and heart disease. The United States Preventive Task Force recommends that adults should be screened for hypertension, hyperlipidemia, and smoking.

6.4 Cerebrovascular disease

GPP Routine screening for cerebrovascular disease by MRI is not recommended.

GPP

The prevalence of silent cerebral infarction in the general population in Singapore is not known. Community-based MRI studies in Western populations have shown the prevalence of silent cerebral infarction to be between 5.8% and 28% depending on age, ethnicity, presence of co-morbidities, and imaging techniques.[153-156] There is no evidence that treatment for silent cerebral infarction in the general population reduces the risk of adverse events.

6.5 Atrial fibrillation

B Opportunistic screening for atrial fibrillation should be routinely performed for all patients by examining the rate and rhythm by pulse palpation, followed by ECG if atrial fibrillation is suspected.[157]

Grade B, Level 2++

The prevalence of atrial fibrillation among Singapore Chinese aged 55 year and above is 1.5%, higher in men, and increasing with age.[158] Atrial fibrillation is associated with a 3- to 4-fold increased stroke risk, approximating 2 to 4% per year.[159-161] Randomized clinical trials have shown the benefit of antithrombotic therapies in reducing the risk of stroke in patients with atrial fibrillation by approximately 60% with adjusted-dose warfarin and by approximately 20% with aspirin.[162] Adjusted-dose warfarin reduces stroke by approximately 45% as compared with aspirin.[161]

Pulse palpation has sensitivity of 94% and specificity of 72% in detecting atrial fibrillation. Patients with an irregular pulse rhythm should then undergo an electrocardiogram.[157]

7 Pre-participation screening for exercise

7.1 Introduction

Pre-participation screening is aimed at reducing the risk of sudden death or injury during exercise. There are three aims in this screening:

- Cardiovascular screening to reduce the risk of sudden death.
- Musculoskeletal screening to identify injuries that need to be managed to prevent aggravation or to identify factors that may predispose the athlete to future injuries.
- Identifying factors that may limit performance, e.g. anaemia, drugs.

Pre-participation screening practices can range from a simple self-administered questionnaire to a full physical examination and investigations. Such practices vary from sport to sport and from country to country. The most systematic and rigorous is that conducted in Italy, where Italian law mandates that every participant engaged in competitive sports activity must undergo a clinical evaluation an obtain eligibility.

7.2 Limitations to general non-selective screening

Since sports injuries and sudden death are often related to underlying medical conditions, the concept of pre-participation screening appears sensible. However, there are limitations to general non-selective screening of a large population[163] namely,

- The very low incidence of underlying conditions that predispose to sudden death and hence the need to screen large populations
- The variety of causes of sudden death, thus requiring different diagnostic tests
- The limited accuracy of available tests results in large numbers of false positive test results, obliging further (usually costly) investigations and possibly leading to the inappropriate exclusion of fit individuals from exercise
- The resources required to screen large populations
- Screening is of limited value in preventing acquired or environmental causes of sudden death or injury due to acute illness, such as heat-stroke, viral infection of the heart (myocarditis) or traumatic injury.

- Some conditions causing sudden death, such as congenital anomalous origin of the coronary arteries, are not usually detectable by simple tests such as the resting or exercise ECG, and require more advanced imaging, such as cardiac MRI or CT angiogram.
- Other causes of sudden death, such as some primary arrhythmias (abnormal heart rhythms) occur in the absence of easily detectable abnormalities of cardiac structure, and hence are not easily diagnosed even with advanced imaging technology.

7.3 Limitations to screening for coronary artery disease in older individuals

In the older population of individuals above the age of 35 years, the most common cause of sudden death is coronary artery disease (coronary artery disease) resulting in acute myocardial infarction. The United States Preventive Services Task Force (USPSTF) examined the use of the resting ECG, exercise ECG test, or EBCT scanning for coronary calcium to screen for coronary artery disease and recommended against routine screening in adults at low risk for coronary artery disease events. They concluded that there was insufficient evidence to recommend for or against routine screening in adults at increased risk for events.[163]

- **The resting ECG** – This is not a useful tool for detection of coronary artery disease since many patients with coronary artery disease have normal resting ECGs and many individuals without coronary artery disease have ECG findings that are suspicious of coronary artery disease, thus unnecessarily raising alarm bells. Approximately one-third to one-half of individuals with a normal coronary arteriogram have ECG abnormalities [33] and approximately 30% of individuals with angiographically proven coronary artery disease have a normal resting ECG.[60] Most coronary events occur in individuals without resting ECG abnormalities.[164]
- **Exercise testing (i.e. exercise stress test)** – This has limited accuracy[165] in an asymptomatic population with a low likelihood of coronary artery disease. In a population with a prevalence of coronary artery disease of 1%, assuming the reported overall specificity of the test is 77%[166], it can be estimated that approximately 97% of 'abnormal' results would be false positive results.
- **CT angiography** – This has higher accuracy than ECG stress testing but is associated with radiation exposure and is not recommended for routine screening of low-risk individuals.

7.4 Pre-participation screening program for young competitive athletes

It is important to remember that, even without a screening program, some individuals may already be identified as being at higher risk owing to pre-existing medical conditions, symptoms, or past episodes of events. There are published reports suggesting that many individuals with exercise-related cardiovascular events had prodromal symptoms that were ignored by the victims or their physician.[167] Maron et al[168] reported in 1996 that of 134 young competitive athletes with sudden cardiac death, in their series, 24 (18%) had probable cardiac symptoms in the 36 months prior to their death. Among adults, 50% of joggers, 75% of squash players, and 81% of distance runners with sudden cardiac death during exercise had probable cardiac symptoms before death.

There is a difference of opinion between the European guidelines and the American Heart Association[163], the American College of Cardiology, and the American College of Sports Medicine with regards to the recommendation of a resting ECG as mandatory in the screening of competitive athletes, based on the limitations of false positives.

In Italy, a compulsory national pre-participation screening program conducted by sports medicine physicians for all young competitive athletes (12 – 35 years of age) has been implemented since 1982 and this has been reported to be successful. In the Veneto region of Italy, this program was able to detect 879 individuals with abnormalities who were subsequently disqualified from competitive sports, including 345 cases of conduction and rhythm abnormalities, 30 cases of hypertrophic cardiomyopathy, 16 cases of arrhythmogenic right ventricular hypertrophy, and 14 cases of dilated cardiomyopathy over a 24-year period[169]. Over the same period, there was a significant and impressive 89% decline in the number of sudden deaths in this region, from 3.6 to 0.4 deaths per 100,000 athletes.[169] There was no change in deaths during this period among the unscreened non-athletes, suggesting that screening mediated the decrease.

In a follow-up report in 2008, Corrado et al[170] recommended the resting ECG be included routinely in the pre-participation screening of young competitive athletes for prevention of sudden cardiac death. Based on a 25-year interval, the mandatory inclusion of the resting ECG has been able to detect asymptomatic individuals with hypertrophic cardiomyopathy and excluded them from competitive sports.

7.5 Risk-stratified pre-participation screening

D Pre-participation screening should be done on risk-stratified groups of athletes.[163, 171-172]

Grade D, Level 4

The Singapore Sports Council's Sports and Safety Committee's Recommendations are[172]:

- Selective screening of the at-risk population, to increase the pre-test probability of identifying the at-risk individuals
- The risk stratification is based on:
  - The individual's intrinsic risk of sudden death or serious injuries (e.g. prodromal symptoms, positive family history)
  - The level of competition (Figure 2)
  - The degree of risk of the particular sport or activity (Table 5)
- Screening protocols that are evidence-based as far as possible, graded according to the degree of risk, and customized to each sport
- Appropriate management of identified at-risk individuals
- Optimization of existing resources
- Minimizing the hindrance to sports participation and sports excellence
- The recognition that pre-participation screening is only part of the strategy to decrease the chance of sudden death and adverse events occurring. Education is the other crucial component of the overall strategy - individuals should be educated on symptoms and signs that require medical attention before embarking on sports activities or exercise.

Besides the level of competition (Figure 2), other factors such as age need to be considered. For example, a 55-year old novice to marathon running may over-zealously undergo high-mileage training without building up to it, and would be considered at risk of sudden death even though he is only a club runner.

Sports activities can also be risk-stratified based on cardiovascular demands (Table 5). Duration of sports participation (e.g. endurance

or ultra-endurance events), contact / collision risk, or environmental stress, can also affect risk, but cardiovascular activity (percentage of maximum aerobic capacity) was chosen as the main factor in this case due to its stronger association with known intrinsic risk factors.

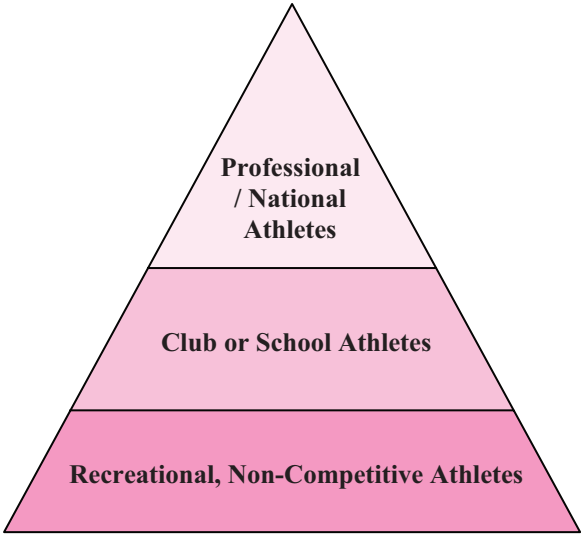
The risk of any physical activity is an interaction of the exercise per se and the individual's fitness and medical conditions. For example, to a fit individual, a category 1 event would be easy whereas to an unfit person with congestive heart failure, a category 1 event may not be tolerable.

Table 5 Categorization of sports based on cardiovascular activity

	Category			
	1	2		
Sport	Bowling Bowls Chess Contract bridge Cuesports Darts Gateball Golf Shooting Sport boules Weiqi Woodball Xiangqi	Archery Badminton Baseball/ Softball Basketball Bodybuilding *Boxing/ wrestling (not an NSA sport) Canoeing Cricket Cycling Dancesport Dragonboat Equestrian Fencing	Field events Floorball Gymnastics Hockey Iceskating Kayaking Lifesaving Martial arts Motor sports Mountaineering Netball Pickleball Powerboat Rollersports	Rowing Running Sailing Sepak takraw Soccer Squash Swimming Table tennis Tennis Triathlon Underwater activities Volleyball Waterski/ wakeboard Weightlifting

Source: Maron et al. 36th Bethesda Conference: Eligibility Recommendations for Competitive Athletes With Cardiovascular Abnormalities. [173]

Figure 2 Athletes' competitive levels



D All sports participants and national athletes should preferably undergo an appropriate level of annual pre-participation screening.[163, 171-172]

Grade D, Level 4

All sports participants and national athletes should preferably undergo pre-participation screening. Some who receive funding to compete in sports may need to undergo compulsory pre-participation screening as a pre-requisite for their funding (much like a pre-employment check up).

D Sports participants involved in strenuous sporting activities, but at a less competitive level than national atheletes, should be encouraged to undergo voluntary pre-participation screening.[172]

Grade D, Level 4

As the pool of club or school athletes is very large, it is not feasible to mandate compulsory annual pre-participation screening in this group. Furthermore, the incidence of sudden death in school athletes is relatively low. Those in category 2 sports (See Table 5) should be strongly encouraged to undergo pre-participation screening.

D Participants in sports and recreational activities should be encouraged to complete a self-administered pre-participation screening questionnaire annually, and consult a doctor if the questionnaire indicates it.[172]

Grade D, Level 4

Participants in sports and recreational activities should be encouraged to complete, a self-administered pre-participation screening questionnaire.[174,175] This should be completed at least annually. Examples of such questionnaires include the PAR-Q questionnaire [Appendix 3A] and The Sudden Arrhythmia Death Syndrome Foundation Questionnaire [Appendix 3B] for children. All individuals involved in sports should take personal responsibility for their own health and to make use of these self-administered questionnaires.

7.6 Screening protocols

D For pre-participation screening, a two- or more stage screening process is encouraged, where the first stage consists of personal and family history taking and physical examination. Based on the findings of the first stage, further tests such as a resting ECG (if not already done), chest X-ray, exercise stress test, echocardiogram, blood investigations, urine tests, etc. may be ordered if indicated.[163]

Grade D, Level 4

Pre-participation screening protocols are aimed at:

- Identifying and excluding individuals with medical contraindications to exercise and sports
- Identifying injuries and risk factors for injuries that may preclude participation in the particular sport
- Identifying conditions that does not exclude an individual from sports participation, but need to be managed in order to safely participate in sports

GPP Abbreviated screening protocols are acceptable in the intervening years between the full screening.

GPP

8 Cost-effectiveness issues

The purpose of cardiovascular screening is to detect in asymptomatic individuals cardiovascular risk factors and disease with the view that early intervention will forestall disease and complications respectively. In this context, three cost effectiveness issues need to be kept in mind.

The first cost effectiveness issue is the ordering of screening tests, to be cost-effective, the tests must be evidence based. Intuitively, the fewer the tests needed to pick out those at risk for intervention, the more cost-saving it will be for whoever is paying for the tests. Detection and treatment of hypertension, hyperlipidemia, diabetes, and smoking, have substantially reduced the incidence of cardiovascular deaths.[176-177] Detecting and treating single risk factors are important.

For those individuals with multifactorial risk factors which individually may not be very high but together place these individuals in the high risk category for coronary artery disease, the cost effective screening strategy is the use of risk scores e.g., the Framingham Risk Score, to identify the high risk asymptomatic individuals.[178] The Framingham Risk Score and other risk scores do not consider obesity, familial history of premature CHD in the first degree relatives, sedentary habit, and psychosocial status. The co-existence of one or several of these complementary risk factors needs consideration that the true global risk is higher than the estimate given by the Framingham or any other score.

There is also the desire to have additional testing to further stratify those individuals with intermediate coronary artery risk scores to see if these individuals should be re-classified as high risk category. These are the new biomarkers. To-date, these new biomarkers have not added much to the traditional markers for routine screening use of detecting asymptomatic individuals with high risk.

The second cost-effectiveness issue is even if costs were not a consideration and the individual were willing to pay for the tests, it should not be assumed that the benefits of screening will outweigh the risks of conducting them e.g. unnecessary radiation effects.

The third cost effectiveness issue is screening without follow-through intervention is ineffective. The purpose of screening is not

achieved until risk reduction action is taken. This point needs to be communicated to the person screened. This point is well illustrated by The Oxcheck[179-180], the British family heart[181], and subsequent studies. The Oxcheck and British family heart studies were separate but concurrent attempts to explore the usefulness of health checks in primary care to reduce heart disease risk. Both studies were population based and nurse led, and both screened several risk factors including blood pressure, cholesterol concentration, smoking habit, weight, and alcohol consumption. Modelling from cost and effectiveness data from these two studies by Wonderling et al (1996)[182] showed that depending on the assumed duration of risk reduction, the programme cost per discounted life year gained ranged from £34,800 for a 1 year duration to £1,500 for 20 years for the British family heart study and from £29,300 to £900 for Oxcheck. In addition, when compared to other health check strategies[183-189] (Table 6) it is clear that the relative cost-effectiveness of the British family heart and Oxcheck studies were critically dependent on the presumed length of effect of the risk reductions from the one year programme. Only if the effect lasts at least five years is the Oxcheck programme likely to be cost-effective; similarly, the effect must last for about 10 years to justify the extra cost associated with the British family heart study.

Table 6 Cost per life year gained of health checks for asymptomatic middle aged men

Nature of intervention (highly cost effective at top of list; less cost effective at bottom)	Subject group	Risk factors used to estimate gains	Model used to extimate gains	Unadjusted cost per life year gained	Unit of cost	Cost per life year gained (1994-5 £UK)
Population based promotion of healthy eating habits[183]	Men aged 40-49	Blood cholesterol concentration	Norwegian cholesterol lowering programme	12	1990 £UK	14
Screening and then dietary advice for hypercholesterolaemia[183]	Men aged 40-64	Blood cholesterol concentration	Framingham logistic equation	65*	1989 $US	48*
Screening and then drugs and dietary advice for hypercholesterolaemia[184]	Men aged 40-64	Blood cholesterol concentration	Framingham logistic equation	306*	1989 $US	230*
Brief advice about smoking during routine GP consultation[185]	Smokers	Smoking status	PREVENT model	613	1992 £UK	650
Brief advice about smoking during routine GP consultation[186]	Men aged 45-50	Smoking status	American Cancer Society 25-state cancer prevention study	748	1984 $US	650
Screening and then drug treatment/lifestyle advice according to degree of hypertension[187]	Adults	Blood pressure	North Karelia Hypertension project and Framingham logistic equation	4 628*	1972-77 $US	7 400*

Nature of intervention (highly cost effective at top of list; less cost effective at bottom)	Subject group	Risk factors used to estimate gains	Model used to extimate gains	Unadjusted cost per life year gained	Unit of cost	Cost per life year gained (1994-5 £UK)
Screening and then drugs and dietary advice according to degree of hypercholesterolaemia[188]	Men aged 50-54	Blood cholesterol concentration	Framingham logistic equation	15 907*	1990? $US	11 200*
Screening and then dietary advice for hypercholesterolaemia[183]	Men aged 40-49	Blood cholesterol concentration	Norwegian cholesterol lowering programme	12 440	1990 £UK	14 600
Screening and then treat optimally+ with antihypertensives[189]	Men aged 45-50	Blood pressure with moderate hypertension	CPPT and Framingham logistic equation	11 400*	1975 $US	18 200*
Screening and then antihypertensives for those with mild to moderate hypertension[189]	Men aged 45-50	Blood pressure	CPPT and Framingham logistic equation	12 900*	1975 $US	20 500*
Screening and then dietary advice/drug treatment for hypercholesterolaemia[183]	Men aged 40-49	Blood cholesterol concentration	Norwegian cholesterol lowering programme	111 549	1990 £UK	130 800

CPPT = Coronary Primary Prevention Trial *Cost per quality adjusted life year gained. +Optimal treatment = treatment according to the most cost effective allocation of resources by blood pressure, age and sex, and between additional treatment versus additional detection.

Source: Wonderling et al (1996): What can be concluded from the Oxcheck and British family heart studies: commentary on cost effectiveness analyses

9 Clinical quality improvement

9.1 Indicators at the national level

	Indicator	Long term target
1.	Proportion of population appropriately screened for hypertension.	85%
2.	Proportion of population appropriately screened for diabetes mellitus.	80%
3.	Proportion of population appropriately screened for hypercholesterolemia.	80%
4.	Proportion of population appropriately screened for coronary artery disease risk using a suitable risk assessment tool.	80%

9.2 Indicators for general practitioners at the clinic level

	Indicator	Long term target
1.	Proportion of regular clinic patients appropriately screened for smoking status at each visit.	90%
2.	Proportion of regular clinic patients aged 18 years and above appropriately screened for BMI and waist circumference annually.	90%
3.	Proportion of regular clinic patients appropriately screened for hypertension within last 2 years.	90%
4.	Proportion of regular clinic patients appropriately screened for diabetes mellitus.	90%
5.	Proportion of regular clinic patients appropriately screened for lipid disorders within last 2 years for those 35 years for men and 45 years for women.	90%
6.	Proportion of patients appropriately screened for coronary artery disease risk using a suitable risk assessment tool.	90%
7.	Proportion of asymptomatic patients screened for coronary artery disease using the electrocardiogram.	0%

Appendix 1A

Testing accuracy and prevalence of a condition

Assumption: A highly accurate test e.g. CT coronary angiography with 95% sensitivity and specificity performed as a screening test in 1000 patients.

The number with coronary artery disease (CAD) is calculated from the prevalence of disease multiplied by the size of the screening population (e.g. 20% prevalence = 200 patients out of 1000). The number with disease detected is based on the sensitivity multiplied by the prevalence of disease. The number of false positives is based on the reciprocal of the specificity multiplied by the number of subjects with no disease (normals) e.g. if there are 800 normals with a specificity of 95%, there will be 5% false positives, 5% x 800 = 40. Percentage false positive = number of false positive/total number of positives (i.e. patients with diagnosed disease plus false positives) x 100.

Prevalence of CAD	20%	10%	5%	1%	0.1%
Number with CAD	200	100	50	10	1
Number with CAD diagnosed	190	95	48	9	1
Number of normals	800	900	950	990	999
Number of false positives	40	45	48	50	approx 50
Total number of abnormal results (false positive plus true positive)	190 + 40 = 230	95 + 45 = 140	48 + 48 = 96	9 + 50 = 59	1 + 50 = 51
Percentage false positive	17% (40/230)	32% (45/140)	50% (48/96)	83% (50/59)	98% (50/51)

From this table, it can be seen that as the prevalence of disease falls, the false positive rate of the test increases, so that at a prevalence of 20%, only 17% of tests are false positives, but at a prevalence of 1%, 83% of tests are false positives. This is true even for an extremely accurate test. Thus, at prevalence of 1%, for every 9 patients detected to have disease, 50 would be misdiagnosed and subjected to further testing.

Appendix 1B

Using a lower cost but less accurate test

Assuming a less accurate test eg ECG stress testing with 68% sensitivity and 77% specificity performed as a screening test in 1000 patients. The number with coronary artery disease is calculated from the prevalence of disease multiplied by the size of the screening population (eg 20% prevalence = 200 patients out of 1000). The number with disease detected is based on the sensitivity multiplied by the prevalence of disease. The number of false positives is based on the reciprocal of the specificity multiplied by the number of subjects with no disease (normals) eg if there are 800 normals with a specificity of 77%, there will be 5% false positives, 5% x 800 = 40. Percentage false positive = number of false positive/total number of positives (i.e. patients with diagnosed disease plus false positives) x 100.

Prevalence of CAD	20%	10%	5%	1%	0.1%
Number with CAD	200	100	50	10	1
Number with CAD diagnosed	136	68	34	7	1?
Number of normals	800	900	950	990	999
Number of false positives	184	207	218	228	230
Total number of abnormal results (false positive plus true positive)	136 + 184 = 320	68 + 207 = 275	218 + 34 = 252	228 + 7 = 235	230 + 1 = 231
Percentage false positive	58% (184/320)	75% (207/275)	87% (218/252)	97% (228/235)	99.5% (231/230)

Using a less accurate test, the results are even worse. As long as the prevalence of coronary artery disease is low, the problem of false positive results persists.

Appendix 2A

Estimation of 10-year coronary artery disease risk for men -- Singapore[1]

Table 2A-1 Estimation of 10-year coronary artery disease risk for men

Age	Points
20 – 34	- 9
35 – 39	- 4
40 – 44	0
45 – 49	3
50 – 54	6
55 – 59	8
60 – 64	10
65 – 69	11
70 – 74	12
75 – 79	13

Allocate points based on person's age, total and HDL cholesterol levels, smoking status and systolic blood pressure (BP). Check the total points against Table 2 for estimate of that person's 10-year CHD risk.

Smoker	Points				
	Age 20 – 39	Age 40 – 49	Age 50 – 59	Age 60 – 69	Age 70 – 79
No	0	0	0	0	0
Yes	8	5	3	1	0

Total cholesterol mmol/ L (mg/ dL)	Points				
	Age 20 – 39	Age 40 – 49	Age 50 – 59	Age 60 – 69	Age 70 - 79
< 4.1 (160)	0	0	0	0	0
4.1 – 5.1 (160 – 199)	4	3	2	1	0
5.2 – 6.1 (200 – 239)	7	5	3	1	0
6.2 – 7.2 (240 – 279)	9	6	4	2	1
≥ 7.3 (280)	11	8	5	3	1

[1] These risk scores are derived from the Framingham-based NCEP ATP III 10-Year Risk Score Tables which have been modified taking into account the Singapore cardiovascular epidemiological data. This modification was carried out as part of a collaboration between investigators at the Singapore Ministry of Health, Singapore General Hospital, National University of Singapore and Prof. Ralph B D'Agostino from the Framingham Heart Study, USA. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285:2486-97.

Appendix 2A

HDL cholesterol mmol/ L (mg/ dL)	Points
≥ 1.6 (60)	- 1
1.3 – 1.5 (50 – 59)	0
1.0 – 1.2 (40 – 49)	1
< 1.0 (40)	2

Systolic BP (mmHg)	Points	
	If untreated	If treated
< 120	0	0
120 – 129	0	1
130 - 139	1	2
140 - 159	1	2
≥ 160	2	3

Table 2A-2 Estimation of 10-year coronary artery disease risk for men

Total points	10-Year Risk (%)		
	Chinese	Malay	Indian
-1	< 1	< 1	1
0	< 1	< 1	1
1	< 1	1	1
2	1	1	1
3	1	1	2
4	1	1	2
5	1	1	3
6	1	2	3
7	2	2	4
8	2	3	5
9	3	4	7
10	4	5	9
11	5	6	11
12	6	8	14
13	8	11	18
14	11	13	> 20
15	13	17	> 20
16	17	> 20	> 20
≥ 17	> 20	> 20	> 20

Appendix 2B

Estimation of 10-year Coronary Artery Disease Risk for Women -- Singapore[2]

Table 2B-1 Estimation of 10-year coronary artery disease risk for women

Age	Points
20 – 34	- 7
35 – 39	- 3
40 – 44	0
45 – 49	3
50 – 54	6
55 – 59	8
60 – 64	10
65 – 69	12
70 – 74	14
75 – 79	16

Allocate points based on person's age, total and HDL cholesterol levels, smoking status and systolic blood pressure (BP). Check the total points against Table 2 for estimate of that person's 10-year CHD risk.

Smoker	Points				
	Age 20 – 39	Age 40 – 49	Age 50 – 59	Age 60 – 69	Age 70 – 79
No	0	0	0	0	0
Yes	9	7	4	2	1

Total cholesterol mmol/ L (mg/ dL)	Points				
	Age 20 – 39	Age 40 – 49	Age 50 – 59	Age 60 – 69	Age 70 - 79
< 4.1 (160)	0	0	0	0	0
4.1 – 5.1 (160 – 199)	4	3	2	1	1
5.2 – 6.1 (200 – 239)	8	6	4	2	1
6.2 – 7.2 (240 – 279)	11	8	5	3	2
≥ 7.3 (280)	13	10	7	4	2

[2] These risk scores are derived from the Framingham-based NCEP ATP III 10-Year Risk Score Tables which have been modified taking into account the Singapore cardiovascular epidemiological data. This modification was carried out as part of a collaboration between investigators at the Singapore Ministry of Health, Singapore General Hospital, National University of Singapore and Prof. Ralph B D'Agostino from the Framingham Heart Study, USA.

Appendix 2B

HDL cholesterol mmol/ L (mg/ dL)	Points
≥ 1.6 (60)	- 1
1.3 – 1.5 (50 – 59)	0
1.0 – 1.2 (40 – 49)	1
< 1.0 (40)	2

Systolic BP (mmHg)	Points	
	If untreated	If treated
< 120	0	0
120 – 129	1	3
130 - 139	2	4
140 - 159	3	5
≥ 160	4	6

Table 2B-2 Estimation of 10-year coronary artery disease risk for women

Total points	10-Year Risk (%)		
	Chinese	Malay	Indian
5	< 1	< 1	1
6	< 1	< 1	1
7	< 1	1	1
8	< 1	1	1
9	1	1	2
10	1	1	2
11	1	2	3
12	1	2	3
13	1	3	4
14	2	4	6
15	3	5	7
16	3	6	10
17	4	8	12
18	5	10	16
19	7	13	20
20	9	16	> 20
21	12	20	> 20
22	15	> 20	> 20
23	19	> 20	> 20
≥ 24	> 20	> 20	> 20

Appendix 3A

Physical Activity Readiness Questionnaire (PAR-Q)

The questionnaire is suitable for those aged between 15 and 69. If you are over 69 years of age, and you are not used to being very active, check with your doctor. Common sense is your best guide in answering these questions. Read the questions carefully and answer each one honestly.

Q1 Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?

Q2 Do you feel pain in your chest when you do physical activity?

Q3 In the past month, have you had chest pain when you were not doing physical activity?

Q4 Do you lose your balance because of dizziness or do you ever lose consciousness?

Q5 Do you have a bone or joint problem that could be made worse by a change in your physical activity?

Q6 Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?

Q7 Do you know of any other reason why you should not do physical activity?

If you answered YES -- If you answered "yes" to one or more questions, talk with your doctor before you start becoming much more active or before you have a fitness test. Tell your doctor about the PAR-Q and which questions you answered "yes".

If you answered NO -- If you answered "no" honestly to all of the questions, you can be reasonably sure that you can start becoming much more physically active or take part in a physical fitness appraisal – begin slowly and build up gradually. This is the safest and easiest way to go.

Things Change -- Even if you answered "no" to all questions, you should delay becoming more active if you are temporarily ill with a cold or a fever, or if you are or may be pregnant. If your health changes so that you then answer "yes" to any of the above questions, tell your fitness or health professional and ask whether you should change your physical activity plan.

Source: PAR-Q and You. Canadian Society for Exercise Physiology. Revised 1994

Appendix 3B

The Sudden Arrhythmia Death Syndrome Foundation Questionnaire

	Yes	No
Has your child fainted or passed out during exercise, emotion or startle?		
Has your child fainted or passed out after exercise?		
Has your child had extreme fatigue associated with exercise (different from other children)?		
Has your child ever had unusual or extreme shortness of breath during exercise?		
Has your child ever had discomfort, pain or pressure in his chest during exercise?		
Has your child ever been diagnosed with an unexplained seizure disorder?		
Are there any family members who had an unexpected, unexplained death before the age of 50 (including SIDS, car accident, drowning)?		
Are there any family members who died of heart problems before the age of 50?		
Are there any family members who have unexplained fainting or seizures?		

Source: http://www.sads.org/images/stories/pdf/assmform.pdf.[174]

Appendix 4A

Criteria for categorisation of screening tests – AM & MOH

1	**Suitable for population-level screening**
	The disease condition is an important health problem; Its natural history is well understood; It is recognisable at an early stage; There is robust evidence (based on meta-analysis of randomised controlled trials, or high-quality ***randomised controlled trials (RCTs)*** available) that use of the screening test improves survival; The target population for the test is the general population at normal risk (although age can be used to stratify this population into risk groups); Recommendations made by trusted expert authorities (e.g. local clinical practice guidelines (CPGs), US Preventive Services Task Force) uniformly support use of screening test; Population-level screening programmes have been implemented successfully elsewhere; Cost-effectiveness data available, based on preferable local, or, if not, overseas data reporting cost effective analysis ratios within the acceptable threshold for Singapore.
2	**Suitable for individual-level decision**
	The disease is recognisable at an early stage; There is some evidence that use of the screening tests improves survival, though not necessarily at same level of robustness; The screening test is not suitable for general populations at normal risk (even after stratification by age into risk groups), although evidence suggests that some more narrowly-defined high-risk groups (defined by other factors such as personal and family history) may benefit; Risk-benefit ratio of benefit to harm is different for different individuals, and may exceed 1 in some groups; Cost-effectiveness data suggest cost effective analysis ratios are above acceptable threshold for Singapore, or there is no cost-effectiveness data.
3	**Not recommended**
	The current evidence is insufficient to assess the balance of benefits and harms of the service; Evidence is lacking, or of poor quality, or is conflicting so that no decision can be made based on the information available. Or: The natural history of the disease is not well understood; There is no easily recognisable early stage of disease; The performance characteristics of the screening test (in terms of sensitivity and specificity) are poor; There is evidence that even narrowly-defined high risk groups will not benefit from the test; The screening test, or follow-up tests arising from a positive screen, are associated with significant medical risks; The risk-benefit ratio consistently exceeds 1 for all members of the population. Recommendations made by trusted expert authorities are uniformly against use of screening test.

Appendix 4B

US Preventive Services Taskforce Recommendation Categories Compared to the AM-MOH Screening Category Framework

	USPSTF		MOH
	Definition	**Suggestions for practice**	**MOH proposed framework**
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.	Equivalent to "Recommended for Population-level screening"
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.	Equivalent to "Recommended for Population-level screening"
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is at least moderate certainty that the net benefit is small.	Offer or provide this service only if other considerations support the offering or providing the service in an individual patient.	Equivalent to "Recommended for Individual-level decision"
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.	Equivalent to "Not recommended"
I Statement (Inconclusive statement)	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.	Equivalent to "Not recommended"

Appendix 4C

List of category 1 screening tests for cardiovascular disease and risk factors

No.	*Screening Test*	*Disease*	*Age Group*
1	Blood pressure measurement	Hypertension	Individuals aged 18 yrs and above
2	Body Mass Index (BMI)	Obesity	Individuals aged 18 yrs and above
3	Fasting blood glucose	Diabetes Mellitus	Individuals aged 40 yrs and above
4	Fasting Lipid	Hyperlipidaemia	Individuals aged 40 yrs and above
5	Waist Circumference	Obesity	Individuals aged 18 yrs and above

List of category 2 screening tests for cardiovascular disease and risk factors

No.	*Screening Test*	*Disease*	*High Risk Group*
1	Abdominal Ultrasonography	Abdominal Aortic Aneurysm (abdominal aortic aneurysm)	Men aged 65 to 75 who have ever smoked
2	Ankle Brachial Index (ABI)	Peripheral vascular disease	Individuals with diabetes mellitus, individual aged 50-70 yrs and is a smoker or with both hypertension and hyperlipidaemia
3	Apolipoprotein A	Coronary artery disease	Individuals with intermediate coronary artery disease risk
4	CT Coronary Artery Calcium Score	Coronary artery disease	Individuals with intermediate coronary artery disease risk
5	ECG	Coronary artery disease	Individuals with intermediate coronary artery disease risk
6	HbA1c	Diabetes Mellitus	Individuals at risk of diabetes mellitus
7	High Sensitivity CRP	Coronary artery disease	Individuals with intermediate coronary artery disease risk

Appendix 4C

No.	*Screening Test*	*Disease*	*High Risk Group*
8	MRI/ MRA brain	Cerebral aneurysm	Individuals with personal or family history of aneurysmal subarachnoid haemorrhage, individuals with autosomal dominant polycystic kidney disease
9	Treadmill Stress Test	Coronary artery disease	Individuals with intermediate coronary artery disease risk

List of category 3 screening tests for cardiovascular disease and risk factors

No.	Screening Test	Disease
1	Apolipoprotein B	Coronary artery disease
2	Homocysteine	Coronary artery disease
3	Duplex Ultrasonography CT Coronary Angiogram	Carotid artery stenosis Coronary artery disease
4	MRI Brain/MRA	Cerebrovascular disease (Stroke)

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category 3A (Self-Study) of the SMC Online CME System. Alternatively, you can claim one CME point under Category 3B (Distance Learning - Verifiable Self Assessment) if you answer at least 60% of the following MCQs correctly. You can submit your answers through the SMJ website at this link: http://smj.sma.org.sg/cme/smj/index.html (*the link will only be available once the Mar 2011 issue of the SMJ becomes available*). The answers will be published in the SMJ May 2011 issue and at the MOH webpage for these guidelines after the period for submitting the answers is over.

Instruction: Indicate whether each statement is True or False.

		True	False
1.	A 50-year-old man underwent health screening. During the counseling session on his results, he asked about the risk factors for cardiovascular disease. Based on the results from the INTERHEART Study, the most harmful risk factor is:		
	A) Dyslipidemia.	☐	☐
	B) Diabetes mellitus.	☐	☐
	C) Hypertension.	☐	☐
	D) Smoking.	☐	☐
2.	A 35-year-old smoker is being counseled on the results of health screening. He wishes to know what the quantum of risk reduction in mortality that he can expect if he were to quit smoking. Based on the results of a Cochrane review of 20 prospective cohort studies, the percentage risk reduction in mortality is:		
	A) 16%	☐	☐
	B) 26%	☐	☐
	C) 36%	☐	☐
	D) 56%	☐	☐

		True	False
3.	A 45-year-old woman describes her diet in a health screening questionnaire on dietary habits, as below. They are within the recommendations of the Singapore Health Promotion Board ABCs of healthy eating.		
	A) Fruits and vegetables – "eating 3 servings of fruits and 1 serving of vegetables daily on average".	☐	☐
	B) Meat and alternatives – "eating 4 servings daily".	☐	☐
	C) Fats, oils, and salt to flavour food – "variable quantities from day to day".	☐	☐
	D) Fluids – "4 to 5 glasses of water per day".	☐	☐
4.	Abdominal obesity is an atherogenic risk factor. The cut off threshold for women based on the Asia-Pacific consensus is:		
	A) equal of more than 78 cm.	☐	☐
	B) equal of more than 80 cm.	☐	☐
	C) equal of more than 88 cm.	☐	☐
	D) equal of more than 90 cm.	☐	☐
5.	The use of glycated haemoglobin (Hba1c) has been advocated by the American Diabetes Association as an additional alternative test for screening and diagnosis of diabetes mellitus. With regards to the guideline on cardiovascular disease and risk factors screening in Singapore, which of the recommendations below is/are true.		
	A) Recommended for screening Caucasians.	☐	☐
	B) Recommended for screening ethnic Chinese.	☐	☐
	C) Recommended for screening Asians.	☐	☐
	D) Not recommended for use as screening or diagnostic test for the time being.	☐	☐

		True	False
6.	In Framingham Risk Score adapted for Singapore use, the following risk factors are included in the calculation of cardiovascular risk.		
	A) Diabetes mellitus.	☐	☐
	B) Smoking.	☐	☐
	C) LDL-cholesterol level.	☐	☐
	D) Diastolic blood pressure.	☐	☐
7.	Mr Tan, aged 46, is asymptomatic. From health screening results he has a blood pressure of 150/100 mmHg, total cholesterol 5.2 mmol/L (200 mg/ml), and HDL 1 mmol/L (40 mg/ml). His eGFR is 55 ml/min. There is no family history of premature cardiovascular disease. He is interested to taking up badminton to keep fit. The following screening tests would be reasonable to consider to further define his cardiovascular risk status.		
	A) CT angiography.	☐	☐
	B) Lp(a) measurement.	☐	☐
	C) Exercise treadmill test.	☐	☐
	D) Natriuretic peptides measurement.	☐	☐
8.	A 65-year-old asymptomatic man presents for health screening. He wishes to know if he should be screened for carotid artery stenosis. The following statements are true regarding asymptomatic carotid artery stenosis and silent cerebral infarction.		
	A) Severe stenosis (>80%) is uncommon in the general Western population (approximately 1%).	☐	☐
	B) Major risk factors for stenosis include advanced age, male gender, hypertension, smoking and hyperlipidemia.	☐	☐
	C) The benefit of carotid endarterectomy can be negated by peri-procedural complications.	☐	☐

		True	False
D)	There is clear evidence that treatment for silent cerebral infarction in the general population reduces the risk of adverse events.	☐	☐

9. In Singapore, the recommendations with regards to pre-participation screening include:

A)	Selective screening of the at-risk population is recommended.	☐	☐
B)	Pre-participation screening can only be conducted by a Sports Physician.	☐	☐
C)	The competitive level of the individual is taken into consideration when deciding if pre-participation screening is necessary.	☐	☐
D)	All school athletes must undergo compulsory pre-participation screening.	☐	☐

10. Pre-participation screening for those who participate in physical activity or intend to participate in physical activity,

A)	Is designed to only detect cardiovascular diseases.	☐	☐
B)	Is limited only to professional athletes.	☐	☐
C)	Has been shown to reduce the incidence of sudden cardiac death in Italy.	☐	☐
D)	Is unnecessary for those under 35 years of age.	☐	☐

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