

Report of the Screening Test Review Committee



ACADEMY OF MEDICINE, SINGAPORE

PATRON: PRESIDENT OF REPUBLIC OF SINGAPORE

Feb 2011

TABLE OF CONTENTS

Content	Page
1. Screening Test Review Committee	3-5
2. Definition and principles of screening	6
3. Background	7
4. Categorisation of screening tests	7-8
5. Report structure	9
6. Part I of Report	10-41
7. Part II of Report	42-50
8. Annex A	51-52
9. Annex B	53
10. Annex C	54
11. Annex D	55-57
12. References	58-64

Screening Test Review Committee

Screening tests are widely available in Singapore, and are provided by both public and private healthcare institutions. In view of the general interest in health screening, a review of the situation would be useful.

A Screening Test Review Committee, consisting of representatives from the Academy of Medicine, Singapore (AMS) and Health Promotion Board (HPB) was set up to provide expert opinion on the appropriate use of specific screening tests.

The composition of the Committee and its Terms of Reference are as follows:

TERMS OF REFERENCE

The Screening Tests Review Committee will:

- A. Develop a Screening Test Framework and make recommendations on the categorisation of commercially-available screening tests within the Screening Test Framework, based on:
 - a. careful review of published scientific evidence; and
 - b. consideration of the overall strength of evidence and the likely benefits and harms that will accrue to the person undergoing such screening

- B. Provide expert opinion on the appropriateness of use of specific screening tests for the early detection of disease, as and when such opinion is needed by Ministry of Health (MOH).

- C. Meet at least once a year to review the current categorisation of screening tests within the Screening Test Framework to ensure continued relevance and appropriateness of the categorisation.

Screening Tests Review Committee

COMMITTEE MEMBERS

Chairman	Prof Lee Hin Peng	Fellow Chapter of Public Health and Occupational Physicians
Members	Prof Chee Yam Cheng	Fellow Chapter of General Physicians College of Physicians, Singapore Past Master (1998-2000) Academy of Medicine Singapore
	A/Prof Terrance Chua Siang Jin	Fellow Chapter Board Member Chapter of Cardiologists College of Physicians, Singapore
	Dr Lee Soo Chin	Fellow Chairperson Chapter of Medical Oncologists College Council Member College of Physicians, Singapore
	A/Prof Sunil Kumar Sethi	Fellow Chapter of Pathologists

Prof Lee Bee Wah	Fellow Immediate Past President (2007 – 2009) College of Paediatrics and Child Health, Singapore
A/Prof Heng Mok Kwee, Derrick	Fellow Chapter of Public Health and Occupational Physicians
Dr Michael Teo Song Kim	Fellow Chapter of Diagnostic Radiologists College of Radiologists, Singapore
Dr Shyamala Thilagaratnam	Director Healthy Ageing Division Health Promotion Board
Dr Tham Tat Yean	CEO and Senior Family Physician Frontier Healthcare Group

Secretariat

Ms Syairah Samsudin	Executive, Professional Affairs Academy of Medicine, Singapore
---------------------	---

With the assistance of

Dr Lim Boon Tar	Medical Officer Epidemiology and Disease Control Division Ministry of Health
Ms Stephanie Seet	Assistant Manager Epidemiology and Disease Control Division Ministry of Health

Definition and Principles of Screening

Definition of Screening

The application of tests or procedures to detect disease early in asymptomatic people

Principles of Screening

Screening persons who are apparently well in order to pick up asymptomatic disease can be beneficial to the individual if early treatment is available to improve the prognosis. It is beneficial to society at large if identification leads to primary and secondary prevention. Wilson and Jungner cited the following principles of screening for early disease detection as a public health programme:

- a) The condition sought should be an important health problem
- b) The natural history of the disease should be adequately understood
- c) There should be a recognisable latent or early preclinical stage
- d) There should be a suitable and acceptable screening test or examination
- e) There should be an accepted treatment or useful intervention for patients with the disease
- f) Facilities for diagnosis and treatment should be available
- g) There should be an agreed policy on whom to treat as patients
- h) The cost of case-finding (including diagnosis and treatment of patients detected) should be economically balanced in relation to possible expenditure on medical care as a whole
- i) Case finding should be a continuing process and not a one-off project.

Whether or not a screening policy results in improved health outcomes depends on a number of factors viz. the characteristics of the disease, the screening test, and the target population.

Screening may be considered where there is a high prevalence of the disease with potential serious consequences, the disease condition has a natural history with a latent stage during which symptoms of disease are either not present or early; and when detected and managed, is beneficial in improving the likelihood of favourable health outcomes (viz. reduced disease-specific morbidity or mortality). The screening test should be acceptable to the public, simple, fairly readily applied, and valid. With regard to diagnosis, the condition must be treatable with treatment and care available for those who need it. Early treatment should improve the outcome compared to treating patients when they present with signs and symptoms of the disease.

There is also a need for screening on a continuing basis rather than single-occasion screening. One-off screening is of limited value because only a small proportion, often those at least risk, is likely to be screened, and screening picks up those persons in the population who just happen at that particular time to have that condition being checked for. It therefore does not affect the future incidence of disease. Continuing examinations at stipulated intervals have greater advantage as they cover more of the population at risk including, by re-examination, persons presenting with new disease.

Background

Given the wide range of medical conditions for which screening is being offered, and the tests available for screening, a framework to categorise screening tests is necessary.

The aim of the screening test framework is to provide clear guidance to doctors, other healthcare professionals and members of the public about the value of specific screening tests and clinical indications. The categorisation is based on a thorough and impartial review of the scientific evidence currently available.

The Screening Test Review Committee has met and decided upon the categorisation of the screening tests based on current clinical evidence, Ministry of Health (MOH) clinical practice guidelines, established overseas clinical guidelines and after taking into account the inputs of the various Chapters and Colleges under the AMS. It will undertake the review on a periodic basis as and when new evidence and perspectives are available.

Categorisation of Screening Tests

A three-category framework for screening tests, with categories of “Not recommended”, “Suitable for individual-level decision” and “Suitable for population-level screening” was used. The criteria for categorisation are detailed in [Annex A](#). [Annex B](#) compares the recommendation categories used by the United States Preventive Services Task Force vis-à-vis the proposed policy framework. [Table 1](#) summarises the definition and possible policy response for each category of screening tests within the framework.

Table 1: Three-Category Framework for Screening Tests

	Category	Definition	Possible policy responses
1	Suitable for population-level screening	There is good robust evidence that the screening test is both clinically effective and cost effective for use to screen the population	Broaden screening coverage as far as possible, by: a) Promoting public education b) Permitting Medisave use c) Providing means-tested subsidies d) Implementing national screening programmes e) Encouraging incorporation of such tests in community and workplace-organised screening
2	Suitable for individual-level decision	The net benefit does not outweigh the risk in general populations, but the screening may be useful for high-risk populations	Medisave use and means-tested subsidies may be considered for some tests where certain high-risk groups of individuals may benefit from the use of the tests. Clear criteria would need to be set, and screening providers monitored to prevent abuse

		OR There is some evidence that the screening test is effective but cost-effectiveness has not been evaluated or the cost effectiveness ratio is unfavourable	Continuing educational programmes for relevant healthcare providers to highlight need to tailor use of tests to individual circumstances
3	Not recommended	a)There is insufficient evidence to make a decision regarding the usefulness of the test b)There is good evidence that the screening test is not effective, or that the net harm outweighs benefits	Patient education programmes to highlight lack of evidence and possible harm of screening using these tests. Continuing educational programmes to inform healthcare providers on the lack of evidence underlying these tests, and emphasise that onus is on the provider to justify the use of these tests in their patients Define standards of care under the National Standards of Care that recommend against use of these tests; physicians will need to justify use of these tests in their patients

This framework is not meant to replace the clinical judgment of physicians as doctors would still need to assess the suitability of specific screening tests for their patients.

For tests listed as Category 1 – ‘suitable for population-level screening’, the categorisation is only applicable for the specified age range. The report describes some circumstances in which specific Category 1 tests could be used outside the specified age range and/or for individuals who are at higher risk for the disease in question. In these situations, the decision should be made on an individual-level basis, based on consultation by a physician [i.e. similar to a Category 2 test “suitable for individual-level decision” (see below)].

High-risk groups may benefit from screening tests listed as “suitable for individual-level decision”. In such cases, screening, including the age at which to start screening and the frequency of screening (if not specified), should be tailored to the individual profile of the patient in such high-risk groups, based on a consultation by a physician.

Report Structure

The report is presented via two axes:

1. By Disease
2. By Type of Tests (e.g. blood test, urine test)

This is to facilitate cross referencing and for the ease of those who would like to check for tests which are available for specific diseases.

In addition, a list of Category 1 and Category 2 screening tests are tabled as Annex C and Annex D respectively for easy reference.

Part I of Report

Categoryisation of the screening tests by disease grouping

- A) Cancer
- B) Heart and Vascular Diseases
- C) Infectious Diseases
- D) Metabolic, Nutritional, Endocrine and Rheumatology Conditions
- E) Musculoskeletal Disorders
- F) Obstetric and Gynaecological Conditions
- G) Vision and Hearing Disorders
- H) Congenital and Paediatric Conditions
- I) Miscellaneous

A) Cancer

1) Breast cancer^{1,8}

1.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Mammogram for women 50-69 years of age

Recommendation: *All normal risk, asymptomatic women 50-69 years of age should be screened with mammography only, every 2 years.*

The underlying premise for breast cancer screening is that it allows for the detection of breast cancers before they become palpable. Small tumours are more likely to be early stage disease, having better prognosis, and are more successfully treated.

Mammography-based screening is widely accepted as appropriate and beneficial for women above the age of 50. Eight randomised controlled trials of screening with mammography have been conducted to date. While there is variation in the observed mortality reductions, a meta-analysis of the most recent results showed a 24% mortality reduction associated with an invitation to screening. There is great variation on recommendations for mammographic screening for women aged 40-49. Therefore, recommendations for Singapore are based on a balance between international guidelines and practice, and the relatively high incidence of breast cancer for Singaporean women in this age group (40% of cases are diagnosed in women below 50 years), while taking into account the weaker evidence, higher costs and higher false positive rate of detecting breast cancer in this age group using screening mammography.

Clinicians can inform women at normal risk aged 40 to 49 years about the potential benefits, limitations and harms associated with screening mammography so that an informed choice can be made. They should base screening mammography decisions on the benefits and harms of screening, as well as on the woman's preferences and breast cancer risk profile. If screening is to be performed, it should be done annually.

Potential risks of mammography include false-positive results, diagnosis and treatment for cancer that would not have become clinically evident during the patient's lifetime, radiation exposure, false reassurance, and procedure-associated problems. False-positive mammography can lead to increased anxiety and to feelings of increased susceptibility to breast cancer, as well as unnecessary diagnostic tests. Women with false negative mammograms may be given false assurance. Up to one-fourth of all invasive breast cancers are not detected by mammography in 40 to 49 years old, compared with one-tenth of breast cancers in 50 to 69 years old. The diagnosis and treatment of breast cancer may be delayed because of a "normal" mammogram.

1.2 Category 2 Screening Tests (Suitable for individual-level decision)

i) Magnetic Resonance Imaging (MRI) Breast

High Risk Group: Proven BRCA carriers, women at high genetic risk for breast cancer

The test is performed annually. Screening should start at age 25-30 years for BRCA mutation carriers and their untested first degree relatives or as early as 5-10 years before the age of onset of breast cancer in the youngest family member in those with family history of breast cancer but no proven mutation.

Women who are at high genetic risk for breast cancer will benefit from annual screening mammography and MRI. Breast MRI should not be used for routine breast screening of women who are at normal risk of developing breast cancer. In women with high genetic risk for breast cancer, studies have shown that MRI detects more cancers (with a sensitivity of 71% to 100%) compared to mammography (sensitivity 25% to 40%). MRI cannot replace mammographic screening in these women as some cancers may manifest as microcalcifications which may not be shown on MRI.

1.3 Category 3 Screening Tests (Not recommended)

- i) Ultrasound Breast (Used in the assessment of a mammographic abnormality, in this case, for females with dense mammograms)
- ii) Tumour marker for breast cancer (e.g. CEA and CA15-3)

2) Cervical Dysplasia/Cervical Carcinoma-In-Situ/Cervical cancer^{1, 8, 26, 35}

2.1 Category 1 Screening Tests (Suitable for population-level screening)

i) Pap smear

Recommendation: All women who have ever had sexual intercourse should undergo screening for cervical cancer from the age of 25 years to 69 years. Pap smear screening should be performed at least once every 3 years.

2.2 Category 3 Screening Tests (Not recommended)

- i) Ultrasound Pelvis
- ii) Computed Tomography (CT) Pelvis

3) Colorectal cancer ^{1, 8, 34, 35}

3.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Faecal immunochemical test (FIT Stool analysis for faecal occult blood)

Recommendation: For average-risk individuals, screening for colorectal cancer should begin at age 50 years. It should be performed annually. Average-risk individuals refer to asymptomatic individuals and individuals who do not have a family history of colorectal cancer, as well as those with family history confined to non-first degree relatives or relatives older than 60 years old.

OR

- ii) Colonoscopy

Recommendation: Colonoscopy is one of the recommended screening tests for the average risk asymptomatic population, from age 50 years. For screening the general population at average risk, colonoscopy should be performed at an interval of no more than 10 years.

For individuals at increased risk or high risk, screening by colonoscopy is also indicated. Please refer to the table below.

Risk Group	Onset (Age)	Frequency of colonoscopy screening
i) Average risk		
Asymptomatic or family history limited to non-first degree relatives	50 yrs	Every 10 yrs
ii) Increased risk		
1. Colorectal cancer in first degree relative (parent, sibling) age 60 yrs or younger or two or more first degree relatives	10 yrs prior to youngest case in the family or age 40 yrs, whichever is earlier	Every 5 yrs
2. Colorectal cancer in first degree relative over the age of 60 yrs	10 yrs prior to youngest case in the family or age 50 yrs, whichever is earlier	Every 10 yrs
3. Personal history of colorectal polyps	3 yrs after polypectomy in the presence of high risk features (>1cm, multiple, villous architecture);	-

	otherwise, 5 yrs after polypectomy for low risk polyps	
4. Personal history of colorectal malignancy	One year after resection	Every 3 yrs
5. Personal history of ovarian or endometrial cancer	One year after resection	-
iii) High risk		
1. Family history of familial adenomatous polyposis	10 to 12 yrs (from puberty)	Annually*
2. Family history of hereditary non-polyposis colorectal cancer	20-25 yrs	Every 1-2 yrs
3. Inflammatory bowel disease a. Left-sided colitis b. Pan-colitis	From 15 th yr of diagnosis From 8 th yr of diagnosis	Every 1-2 yrs Every 1-2 yrs

*Flexible sigmoidoscopy from age 10-12 years (puberty) until adenomas are identified, upon which screening is switched to colonoscopy

3.2 Category 2 Screening Tests (Suitable for individual-level decision)

i) Computed Tomography (CT) Colonography

Recommendation: For individuals above 50 years not going for colonoscopy or FIT screening. If the initial screening study with CT colonography is negative, a screening interval of 5 years is recommended.

CT colonography, also known as virtual colonoscopy, is a minimally invasive imaging examination of the colon and rectum, using CT scan to acquire images and computer software to process the images for interpretation. It is the best available imaging test if optical colonoscopy is contraindicated or incomplete; and has been shown to be effective in detecting neoplasms ≥ 10 mm, and is recommended for individuals above 50 years, if not going for colonoscopy or FIT screening.

3.3 Category 3 Screening Tests (Not recommended)

i) Carcinoembryonic antigen (CEA)

ii) Abdominal X-ray (AXR)

iii) CT Abdomen

4) **Endometrial cancer** ^{26, 35}

4.1 Category 3 Screening Tests (Not recommended)

- i) Ultrasound Pelvis
- ii) CT Pelvis

5) **Gastric cancer** ³³

5.1 Category 3 Screening Tests (Not recommended)

- i) Oesophago Gastro Duodenoscopy (OGD)

6) **Liver cancer (Hepatocellular carcinoma)** ⁸

6.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Alpha-FoetoProtein (AFP)

High Risk Groups: Hepatitis B carrier or individuals with liver cirrhosis

The test should be performed annually. There is no definite recommended age to start surveillance although local statistics show that hepatocellular carcinoma incidence increases from the age of 30 years in males and 35 years in females.

Patients with chronic hepatitis B infection or liver cirrhosis from other aetiologies are at increased risk of developing hepatocellular carcinoma, and surveillance should be offered to these at-risk individuals with the aim of detecting hepatocellular carcinoma that could be more amenable to therapy, and hence potentially leading to better outcomes.

A rise in alpha-foetoprotein level (>20 ng/ml) in the absence of significant liver inflammation suggests hepatocellular carcinoma with a negative predictive value of 99% and a positive predictive value of up to 30% in non-cirrhotics and 60% in cirrhotics. A rising trend strongly suggests the presence of hepatocellular carcinoma, although alpha-foetoprotein should never be used alone to diagnose hepatocellular carcinoma.

- ii) Ultrasound Hepatobiliary System (US HBS)

High Risk Groups: Hepatitis B carrier or individuals with liver cirrhosis

The test should be performed annually. There is no definite recommended age to start surveillance although local statistics show that hepatocellular carcinoma incidence increases from the age of 30 years in males and 35 years in females.

The sensitivity of ultrasonography of the liver ranges from 58-87% in cirrhotics to 71-90% in non-cirrhotics, with a false positive rate of 28-82%.

Regenerating and/or dysplastic nodules in cirrhosis are the leading cause of false-positive ultrasonography of the liver.

6.2 Category 3 Screening Tests (Not recommended)

- i) Liver Function Test (LFT)

7) Lung cancer^{1, 8}

7.1 Category 3 Screening Tests (Not recommended)

- i) Tumour marker for lung cancer
- ii) Chest X-ray (CXR)
- iii) Spiral CT scan – Evidence currently under review

Evidence for screening in high risk groups is currently under review and the Committee may upgrade the test to Category 2 (suitable for individual-level decision) once the latest published trials/evidences are available and the high-risk groups have been properly defined.

8) Nasopharyngeal carcinoma (NPC)⁸

8.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Tumour marker for NPC (EBV-EA-EBNA-1)

High Risk Groups:

- a) individuals with a first degree relative (parent, sibling) with NPC
- b) individuals with 2 or more relatives with NPC

Familial aggregation of NPC is well documented in many epidemiological studies. Between 6.0-15.5% of newly diagnosed NPC patients will have a family history of NPC. In many studies and follow-up reports, first degree relatives have increased risk compared to the general population in the same age groups. This magnitude of familial risk in endemic regions is one of the highest among cancers. Family history by itself has no actual clinical effect on the survival, but serves to advance NPC diagnosis among those with diseased relatives.

- ii) Nasoscopy

High Risk Groups:

- a) individuals with a first degree relative (parent, sibling) with NPC
- b) individuals with 2 or more relatives with NPC

9) **Oesophageal cancer**³³

9.1 Category 3 Screening Tests (Not recommended)

- i) OGD

10) **Ovarian cancer**^{1, 8, 26, 35}

10.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Transvaginal Ultrasound

High Risk Group: BRCA-Carrier

Transvaginal ultrasound is recommended in women with or at high risk for BRCA mutations based on expert consensus.

10.2 Category 3 Screening Tests (Not recommended)

- i) Cancer antigen (CA) 125
- ii) CT Pelvis

11) **Pancreatic cancer**¹

11.1 Category 3 Screening Tests (Not recommended)

- i) CA 19-9

12) **Prostate cancer**^{1, 8, 36}

12.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Prostate-Specific Antigen (PSA)

Men who are between 50 and 75 years of age, with an estimated life expectancy of more than 10 years, may be offered screening for prostate cancer after a discussion of both the potential benefits and harms associated with prostate cancer screening.

High Risk Groups:

High-risk men, such as men with a strong family history of prostate cancer, i.e. one or more first-degree relatives (father, brother) diagnosed before age 65 years, may be offered screening at an earlier age.

In general, prostate specific antigen screening is done on an annual basis. However, this screening may be performed once every 2 years in low risk men with baseline prostate specific antigen less than 1.0 ng/ml. Due to the uncertainty that PSA testing results in more benefit than harm, a thoughtful and broad approach to PSA is critical. The decision to use PSA for

the early detection of prostate cancer should be individualised. Patients need to be informed of the risks and benefits of testing before it is undertaken.

Prostate cancer survival is related to many factors, especially the extent of tumour at the time of diagnosis. The 5-year relative survival among men with cancer confined to the prostate (localised) or with just regional spread is 100 percent, compared with 31.9 percent among those diagnosed with distant metastases. While men with advanced stage disease may benefit from palliative treatment, their tumours are generally not curable.

Thus, a screening programme that could identify asymptomatic men with aggressive localised tumours might be expected to substantially reduce prostate cancer morbidity, including urinary obstruction and painful metastases, and mortality.

Although prostate biopsies rarely cause complications serious enough to require hospitalisation, screening is not an entirely benign process and may be associated with discomfort and possible complications of biopsy. In addition, false-positive results have a psychological cost. Chronic anxiety can also follow a negative prostate biopsy because this apparently favourable result cannot completely rule out prostate cancer given the relatively high false-negative biopsy rate.

12.2 Category 3 Screening Tests (Not recommended)

- i) MRI prostate

13) Testicular cancer¹

13.1 Category 3 Screening Tests (Not recommended)

- i) Testicular cancer test (e.g. AFP and beta-HCG)

B) Heart and Vascular Diseases

1) Abdominal Aortic Aneurysm (AAA)^{1, 10}

1.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Abdominal Ultrasonography

High Risk Group: Men aged 65 to 75 years who have ever smoked

The United States Preventive Services Task Force (USPSTF) found good evidence that screening for AAA and surgical repair of large AAAs (5.5 cm or more) in men aged 65 to 75 years who have ever smoked (current and former smokers) leads to decreased AAA-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 AAA. 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 USPSTF concluded that the benefits of screening for AAA in men aged 65 to 75 years who have ever smoked outweigh the harms.

2) **Cerebral aneurysm**⁵⁸

2.1 Category 2 Screening Tests (Suitable for individual-level decision)

i) MRI/ Magnetic Resonance Angiography (MRA) brain

High Risk Groups:

- a) Individuals with a history of aneurysmal subarachnoid haemorrhage
- b) Individuals with autosomal dominant polycystic kidney disease
- c) Individuals who have two or more first-degree relatives (parent, sibling) with documented subarachnoid haemorrhage

Unruptured intracranial aneurysms occur in up to 6 percent of the general population. Most persons with these aneurysms remain asymptomatic and are usually unaware of their presence.

Subarachnoid haemorrhage associated with aneurysmal rupture is a potentially lethal event with a mortality rate as high as 50 percent. Many patients who survive the initial haemorrhage have permanent disability. In patients with a history of aneurysmal subarachnoid haemorrhage, the annual rate of new aneurysm formation is between 1 and 2 percent, and the risk of aneurysmal rupture appears to be increased. Therefore, surveillance of these patients with magnetic resonance angiography may be justified.

Screening should also be considered in patients with some rare conditions (e.g., autosomal dominant polycystic kidney disease) that are associated with an increased risk of aneurysms.

Patients with one affected first-degree relative should be differentiated from those with more than one such relative. Based on literature review, the Stroke Council of the American Heart Association does not recommend screening for aneurysms in patients who have only one first-degree relative with aneurysmal subarachnoid haemorrhage. The decision on whether or not to screen for intracranial aneurysms in patients who have two or more first-degree relatives with documented subarachnoid haemorrhage is best decided on a case-by-case basis.

3) **Cerebrovascular disease (Stroke)**¹⁰

3.1 Category 3 Screening Tests (Not recommended)

- i) MRI/ MRA brain

4) **Carotid artery stenosis**^{1, 10}

4.1 Category 3 Screening Tests (Not recommended)

- i) Duplex Ultrasonography

5) **Coronary Heart Disease (CHD)**^{1, 10, 11, 37, 38, 39, 66, 67}

5.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Electrocardiography (ECG)

Recommendation: The resting 12-lead ECG provides valuable information about myocardial ischemia in symptomatic patients who have known coronary heart disease, and may assist in the evaluation of atypical chest pain. However, there is presently no evidence that the routine ambulatory ECG provides reliable information concerning ischemia in asymptomatic subjects who do not have known coronary heart disease.

ECG may be performed in asymptomatic hypertensive patients, when:

- a. Evaluating for target end-organ damage (Left ventricular hypertrophy)
- b. New symptoms or signs develop (chest pain, breathlessness, palpitations, new murmurs or signs of heart failure or arrhythmia).
- c. During initiation of medication that might alter QT intervals or has proarrhythmic effect.

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

- ii) High-Sensitivity C-Reactive Protein (hs CRP)

Recommendation: C-Reactive Protein (CRP) does not appear to be directly atherogenic. When measured using a high sensitivity assay, hsCRP is a marker of inflammation, and may potentially identify asymptomatic individuals at risk for acute coronary events. Restricted and judicious use of hsCRP measurement is suggested for health screening.

The decision to measure hsCRP should only occur after a global risk assessment of coronary heart disease, and considered only if the result will

change the patient's management (e.g. assist in the decision to initiate lipid therapy):

- a) If the 10-year predicted risk is <5%, hsCRP should not be measured.
- b) 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).
- c) If risk is intermediate (10%–20%) and uncertainty remains as to the use of preventive therapies such as statins or aspirin, then hsCRP measurement might be useful for further stratification into a higher or lower risk category.

hsCRP using standardised assays categorises 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 \geq 10.0 mg/L.

iii) Apolipoprotein A

Recommendation: Apolipoprotein A determination is not recommended for routine cardiovascular disease screening. After global risk assessment, Apolipoprotein A measurement in patients with a strong family history of premature cardiovascular disease may be useful for identifying individuals having a genetic predisposition to cardiovascular disease.

iv) CT Coronary Calcium Score

Recommendation: In selected situations, it is reasonable to consider individualised use of coronary artery calcium score (CACS), when the information provided by the CACS will help to guide the patient's management (e.g. decide on initiation of lipid therapy), and after a global risk score has been performed. For example:

- (a) Asymptomatic patients with intermediate CHD 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.

The American College of Cardiology Foundation (ACCF) and American Heart Association (AHA) Expert Consensus Document on Coronary Artery Calcium Scoring judged that it may be reasonable to consider use of CACS

measurement in asymptomatic patients with intermediate CHD 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 score, and subsequent patient management may be modified in patients with low CHD risk. The same expert document does not recommend use of CACS measurement in low CHD risk (below 10% 10-year risk of estimated CHD events).

In asymptomatic patients with high CHD risk (greater than 20% estimated 10-year risk of estimated CHD events, or established coronary disease, or other high-risk diagnoses) the expert document does not advise CACS 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. For this reason, unselected screening of individuals without prior consideration of the global risk score, or whether the CACS will alter management is not encouraged.

There is also currently no evidence to recommend repeat testing of CACS to assess progression of atherosclerosis.

v) Treadmill Stress Test

Recommendation: In selected individuals, screening for CAD with treadmill stress test may be undertaken on an individualised basis.

For example:

- (a) The evaluation of 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
 - are at high risk for CAD because of other diseases
- (b) The evaluation of asymptomatic persons with diabetes who plan to start vigorous exercise.

Because of the limited specificity of exercise stress testing, there is a likelihood of false positive results when treadmill testing is carried out in a low

risk population, which then can lead on to further testing with stress imaging or coronary angiography to allay concerns. This should be explained to the patient prior to testing.

5.2 Category 3 Screening Tests (Not recommended)

- i) CT coronary angiogram
- ii) Apolipoprotein B
- iii) Homocysteine
- iv) Serum uric acid

6) Peripheral Vascular Disease (PVD)^{1, 10}

6.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Ankle Brachial Index (ABI)

High Risk Groups:

- a) Asymptomatic people with diabetes mellitus
- b) Any individual aged 50-70 years and is a smoker
- c) Any individual aged 50-70 years with both hypertension and hyperlipidaemia

ABI is a test for peripheral vascular disease which has been shown to be associated with CAD. The attraction of ABI 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. As with any screening test, it should be considered after global risk scoring and when the result of testing is likely to alter management. Despite the potential value of ABI, a recent randomised trial of the use of aspirin in patients with abnormal ABI did not show any benefit.

C) Infectious Diseases

1) Human Immunodeficiency Virus Infection (HIV)^{1, 4, 13}

1.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) HIV screen

High Risk Groups:

- a) all pregnant women

- b) men who have had sex with men
- c) men and women having unprotected sex with multiple partners
- d) past or present injection drug users
- e) men and women who exchange sex for money or drugs
- f) individuals whose past or present sex partners were HIV-infected, bisexual, or injection drug users
- g) persons being treated for sexually transmitted diseases (STDs)
- h) persons who have had blood transfusion

Pregnant women should be offered the test in the first trimester because timely institution of anti-retroviral therapy can prevent mother-to-child HIV transmission.

Persons who continue to exhibit high-risk behaviour should have screening tests on a regular basis. The frequency at which these individuals are screened is a matter of clinical discretion. Screening for HIV should be performed 6-monthly in a person who continues to exhibit high-risk behaviour. Persons with recent high-risk behaviour should be screened at 1 month and 3 months after the last high-risk exposure to rule out a possible initial false negative result.

The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians screen for human immunodeficiency virus (HIV) in all adolescents, adults at increased risk for HIV infection and all pregnant women.

The USPSTF found good evidence that appropriately timed interventions, particularly highly active antiretroviral therapy (HAART), lead to improved health outcomes for many of those screened, including reduced risk for clinical progression and reduced mortality. Since false-positive test results are rare, harms associated with HIV screening are minimal. Potential harms of true-positive test results include increased anxiety, labeling, and effects on close relationships. Most adverse events associated with HAART, including metabolic disturbances associated with an increased risk for cardiovascular events, may be ameliorated by changes in regimen or appropriate treatment.

The USPSTF concluded that the benefits of screening individuals at increased risk substantially outweigh potential harms.

The USPSTF also found good evidence that introduction of universal prenatal counselling and voluntary testing increases the proportion of HIV-infected women who are diagnosed and are treated before delivery. There is good evidence that recommended regimens of HAART are acceptable to pregnant women and lead to significantly reduced rates of mother-to-child transmission.

Early detection of maternal HIV infection also allows for discussion of elective caesarean section and avoidance of breastfeeding, both of which are associated with lower HIV transmission rates.

There is no evidence of an increase in foetal anomalies or other foetal harm associated with currently recommended antiretroviral regimens (with the exception of efavirenz). Serious or fatal maternal events are rare using currently recommended combination therapies. The USPSTF concluded that the benefits of screening all pregnant women substantially outweigh potential harms.

2) Hepatitis A infection^{1, 13, 18, 19}

2.1 Category 3 Screening Tests (Not recommended)

- i) Hepatitis A screen

3) Hepatitis B infection/Hepatitis B carrier^{1, 4, 13}

3.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Hepatitis B screen

High Risk Group: All pregnant women

Special consideration: Foreigners and immigrants from countries where Hepatitis B virus (HBV) are endemic should also be considered for screening.

All pregnant women should be tested for Hepatitis B surface antigen (HBsAg) during early antenatal visit, preferably during the first visit.

The USPSTF found good evidence that universal prenatal screening for HBV infection using HBsAg substantially reduces prenatal transmission of HBV and the subsequent development of chronic HBV infection. The current practice of vaccinating all infants against HBV infection and postexposure prophylaxis with hepatitis B immune globulin administered at birth to infants of HBV-infected mothers substantially reduces the risk for acquiring HBV infection.

4) Hepatitis C infection^{1, 13}

4.1 Category 3 Screening Tests (Not recommended)

- i) Hepatitis C Screen

The USPSTF found no evidence that screening for Hepatitis C infection in adults at high risk leads to improved long term health outcomes, although the yield of screening would be substantially higher in a high-risk population than in an average-risk population and there is good evidence that anti-viral therapy improves intermediate outcomes, such as viraemia. There is, as yet, no evidence that newer treatment regimens for Hepatitis C infection, such as pegylated interferon plus ribavirin, improve long-term health outcomes.

5) **Intestinal parasitic infection**¹⁷

5.1 Category 2 Screening Tests (*Suitable for individual-level decision*)

- i) Stool for ova, cyst and parasites

Special consideration: New immigrants from countries with high prevalence of such diseases should be considered for screening.

Asymptomatic international travellers, who have been abroad for many months or longer, particularly in resource limited settings, could be screened for certain diseases, including stool examination for ova and parasites.

6) **Rubella**^{1, 13, 20}

6.1 Category 2 Screening Tests (*Suitable for individual-level decision*)

- i) Rubella serology

High Risk Group: All pregnant women should be screened for rubella susceptibility during their first clinical encounter.

The American Academy of Pediatrics (AAP), American College of Obstetricians and Gynaecologists (ACOG) and Advisory Committee on Immunization Practices (ACIP) recommend routine prenatal or antepartum serologic screening of all pregnant women and postpartum vaccination of those found to be susceptible.

7) **Syphilis**^{1, 4, 13, 27}

7.1 Category 2 Screening Tests (*Suitable for individual-level decision*)

- i) Venereal Disease Research Laboratory test (VDRL)

High Risk Groups:

- a) All pregnant women
- b) Men who have sex with men and engage in high-risk sexual behaviour
- c) Commercial sex workers
- d) Persons who exchange sex for drugs
- e) Persons diagnosed with other sexually transmitted diseases (STDs) (i.e., Chlamydia, gonorrhoea, genital herpes simplex, human papilloma virus, and HIV) or with genital ulceration

The optimal frequency of screening is a matter of clinical discretion. Screening for syphilis should be performed 1 month after exposure, and repeated again after 3 months for high risk groups as defined by (b) to (e) above.

The Centres for Disease Control and Prevention (CDC) recommend obtaining serology for syphilis from all women at the first antenatal visit. Routine screening for all pregnant women is justified in view of the severe neonatal morbidity and mortality associated with congenital syphilis, as well as its potential preventability. There is evidence from several studies which demonstrate that prenatal screening for syphilis is cost-effective.

The U.S. Preventive Services Task Force (USPSTF) also strongly recommends that clinicians screen persons at increased risk for syphilis infection and all pregnant women.

Although the USPSTF found no new direct evidence that screening for syphilis infection leads to improved health outcomes in persons at increased risk, there is adequate evidence that screening tests can accurately detect syphilis infection and that antibiotics can cure syphilis. Screening may result in potential harms (such as clinical evaluation of false-positive results, unnecessary anxiety to the patient, and harms of antibiotic use). The USPSTF concludes that the benefits of screening persons at increased risk for syphilis infection substantially outweigh the potential harms.

8) Tuberculosis (TB)^{1, 4, 13}

8.1 Category 2 Screening Tests (Suitable for individual-level decision)

i) Chest X-ray (CXR)

High Risk Group: Close contacts of tuberculosis (family members who live together)

Special consideration: Foreigners and employees from countries where the disease is highly prevalent.

Close contacts of infectious TB patients, specifically family members who live together, should also undergo screening for latent (hidden) TB infection. This helps to identify persons for treatment to prevent the progression of latent TB to active TB disease.

D) Metabolic, Nutritional, Endocrine and Rheumatology Conditions

1) Anaemia (Iron-deficiency anaemia)^{1, 13, 14}

1.1 Category 2 Screening Tests (Suitable for individual-level decision)

i) Full Blood Count (FBC)

High Risk Groups:

- a) Pregnant women
- b) Non-pregnant women of childbearing age
- c) Preterm infants and low birth weight infants
- d) Infants who are fed a diet of non-iron-fortified infant formula for >2 months
- e) Breast-fed infants who do not consume a diet adequate in iron after age 6 months (i.e., who receive insufficient iron from supplementary foods)
- f) Children who have special health-care needs (e.g. children who use medications that interfere with iron absorption and those who have chronic infection, inflammatory disorders, restricted diets, or extensive blood loss from a wound, an accident, or surgery).

All pregnant women should be screened at the first prenatal visit; for non-pregnant women of child-bearing age, they should be screened once before pregnancy. For infants and children at high risk as defined from (c)-(f), the frequency is once a year until 5 years old.

The US Preventive Services Task Force concludes that the benefits of routine screening for iron deficiency anemia in asymptomatic pregnant women outweigh the potential harms. The Centers for Disease Control and Prevention (CDC) also recommend screening for iron deficiency anemia in high-risk infants, high-risk preschool children, pregnant women, and non-pregnant women of childbearing age.

2) **Diabetes Mellitus**^{1, 7, 15, 16}

2.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Fasting blood glucose

Recommendation: *Screening should begin at age 40 years, and be considered at an earlier age (e.g. 30 years) if any of the risk factors for diabetes is present. Subsequently, screening should be carried out every three years for those with normal glucose tolerance and annually for those with impaired fasting glycaemia (IFG) or impaired glucose tolerance (IGT).*

Risk factors for Diabetes Mellitus include (any one of the following):

- Overweight/obesity (body mass index >25.0 kg/m²)
- Hypertension (>140/90 mmHg)
- A first degree relative (parent, sibling) with diabetes mellitus
- Previous gestational diabetes mellitus

- Coronary heart disease
- Polycystic ovary disease
- Dyslipidaemia (HDL cholesterol <1.0 mmol/l, and/or triglyceride level >2.30 mmol/l)
- Previously identified impaired fasting glycaemia (IFG) or impaired glucose tolerance (IGT)

2.2 Category 3 Screening Tests (Not recommended)

- Glycosylated haemoglobin (HbA1c) – Evidence currently under review

The latest recommendation from the American Diabetes Association (ADA) in January 2010 states that HbA1c is suitable for diagnosing and screening Diabetes Mellitus and pre-diabetes. This contradicts an earlier report from World Health Organisation (WHO) in 2006 which did not recommend the test as a suitable diagnostic test for diabetes or intermediate hyperglycaemia.

Although HbA1c is not recommended as a diagnostic test for diabetes by WHO, there is ongoing work to standardise HbA1c reporting worldwide which may lead to further developments in the role of HbA1c. Evidence is currently under review at WHO using the recently adopted GRADE system of evaluating the evidence and recommendations appropriate for a global audience will be formulated and published.

3) Diabetic microalbuminuria / albuminuria / nephropathy⁷

3.1 Category 2 Screening Tests (Suitable for individual-level decision)

- Urine Microalbumin/Creatinine Ratio

Recommendation: Screening for albuminuria should begin at 5 years after the diagnosis of type 1 diabetes. It should, however, begin immediately with the diagnosis of type 2 diabetes. Thereafter, screening for albuminuria should be done annually.

Kidney disease develops in a similar, though not identical fashion in type 1 and type 2 diabetes mellitus, with progressive proteinuria heralding the development of nephropathy. Less commonly, however, renal dysfunction may occur in the absence of the classic progressive albuminuria.

Microalbuminuria (defined as low levels of urine albumin from 30 to 299 mg/day) develops in 40% of type 1 diabetic patients about 5 years after initial presentation. When microalbuminuria is due to diabetic nephropathy, it is persistent. Without specific interventions, 80% will progress to a stage of clinical proteinuria over a period of 10 to 15 years, where the urine albumin levels are >300 mg/l. End stage renal disease (ESRD) usually occurs in 50%

of type 1 diabetes with overt nephropathy within 10 years, and in more than 75% by 20 years.

A higher proportion of type 2 diabetic patients may have proteinuria at the time of diagnosis of hyperglycaemia, as the onset of development of hyperglycaemia is usually not distinct like it is with type 1 diabetes. Without specific interventions, a smaller proportion (20-40%) with microalbuminuria will progress to overt nephropathy, but only about 20% of these patients would have progressed to ESRD within 20 years.

4) **Gout**^{50, 51, 52}

4.1 Category 3 Screening Tests (Not recommended)

- i) Serum uric acid

5) **Hyperlipidaemia**^{4, 6}

5.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Fasting Lipids

Recommendation: *Screening should be carried out in all individuals aged 40 years and above. If the results are within optimal range, screening should be repeated at 3 yearly intervals. Screening should be considered at an earlier age if risk factors for hyperlipidaemia are present. For at-risk individuals, screening should be repeated more frequently.*

In summary, the following groups are to be screened:

- a. All individuals aged 40 years and above
- b. All adults with pre-existing coronary heart disease, cerebrovascular or peripheral artery disease irrespective of age
- c. All adults with diabetes mellitus irrespective of age
- d. All adults with impaired fasting glycaemia or impaired glucose tolerance irrespective of age
- e. All adults with a family history and/or clinical evidence of familial hyperlipidaemia

6) Hypertension^{4, 40, 41}

6.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Blood pressure measurement

Recommendation: 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 BP). Measurements are recommended annually for persons with a diastolic blood pressure of 80-89 mmHg or systolic blood pressure of 130-139 mmHg (i.e. high normal BP). Persons with higher blood pressures or a major coronary risk factor such as diabetes mellitus require more frequent measurement.

7) Kidney disorder (Kidney dysfunction)^{9, 59, 60}

7.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Kidney function test/Renal panel

Recommendation: Individuals at increased risk of developing chronic renal disease should undergo testing of serum creatinine in order to estimate the glomerular filtration rate.

High Risk Groups (Any one of the following risk factors):

- a) Any individual with Diabetes Mellitus (DM)
- b) Any individual with Hypertension (HTN)
- c) Any individual with cardiovascular disease
- d) Any individual aged 50 years and above and who is a smoker
- e) Any individual with a family history of end-stage renal disease (ESRD)

The test is performed annually.

The US Multiple Risk Factor Intervention Trial had showed that older age, smoking, hypertension and diabetes were significant risk factors for end stage renal disease. Familial aggregation of renal disease, in excess of that predicted by clustering of diabetes and hypertension, had also been reported in a population-based case-control study. In view of this, individuals with any one of the mentioned risk factors should be considered for screening.

The National Kidney Foundation has more than 10 years of field experience with the Kidney Early Evaluation Programme (KEEP), a targeted screening programme directed at the general population with diabetes, hypertension or family history of kidney diseases. The criteria for high-risk groups were developed in the mid-1990s based on diabetes and hypertension being the

leading cause of end-stage renal disease (ESRD), accounting for 71% of all cases, and on increased ESRD rates in family members of dialysis patients.

ii) Urine analysis

Screening using dipstick analysis should be performed for the following individuals at risk for kidney disease:

High Risk Groups (Any one of the following risk factors):

- a) Any individual with Diabetes Mellitus (DM)
- b) Any individual with Hypertension (HTN)
- c) Any individual with cardiovascular disease
- d) Any individual aged 50 years and above and who is a smoker
- e) Any individual with a family history of end-stage renal disease (ESRD)

Screening to detect microscopic haematuria and proteinuria in asymptomatic population is not recommended. However, screening using dipstick analysis should be done for individuals at risk for kidney disease.

8) **Obesity**^{1, 3, 4}

8.1 Category 1 Screening Tests (Suitable for population-level screening)

i) Body Mass Index (BMI)

Recommendation: *All individuals 18 years of age or older should be screened annually*

ii) Waist Circumference

Recommendation: *All individuals 18 years of age or older should be screened annually.*

8.2 Category 3 Screening Tests (Not recommended)

i) Body fat measurement

9) **Osteoporosis/ osteopenia**^{1, 4, 12, 71, 72}

9.1 Category 2 Screening Tests (Suitable for individual-level decision)

i) Bone mineral density scan (BMD)

High risk group: Individuals with high Osteoporosis Self-assessment Tool for Asians (OSTA) score.

It is not advisable to screen BMD in the whole population though the definition of osteoporosis is based on BMD, as the measurements are costly and the cost-benefit or cost-effectiveness of such a strategy has not been demonstrated.

For females, the Osteoporosis Self-Assessment Tool (OSTA) for Asians should be used as a screening tool first before deciding on whether BMD should be offered. The Osteoporosis Self-assessment Tool for Asians (OSTA), which is based on *age* and *weight*, categorises *postmenopausal* Asian women into high, moderate and low risk of having osteoporosis on subsequent BMD measurement.

A case-finding approach should be employed for women falling into the moderate risk category and they should be evaluated for clinical risk factors, and have BMD measured if these factors are present. The prevalence of osteoporosis is low enough in the low risk category for BMD to be deferred, unless the woman has other identified clinical risk factors.

Women with osteoporosis, who are being monitored for progression or who are being treated, should have a follow-up BMD, usually at an interval of at least one year. In women with osteopenia (BMD between 1 and 2.5 S.D. below the mean peak bone mass of young adults) a reasonable interval might be 1 to 2 years, while in those with normal BMD (more than -1 S.D. below the mean peak bone mass of young adults) a more reasonable interval may be 2 to 5 years.

OSTA formula (for females): Applicable for Asian females who are postmenopausal

Age (years) – weight (kg) =

> 20 high risk (should screen with BMD)

0-20 moderate risk (screen with BMD if other risk factors for osteoporosis present)

< 0 low risk

Risk factors for low bone mass for which BMD measurement might be considered are as follows:

Non-modifiable risk factors

- Personal history of previous fracture as an adult
- History of fracture in a first degree relative (especially maternal)
- Low body weight
- Older age

Potentially modifiable risk factors

- Current cigarette smoking
- Alcohol abuse
- Early natural or surgical menopause before the age of 45 years, or prolonged premenopausal amenorrhea lasting > 1 year
- Drugs e.g. corticosteroids (equivalent to prednisolone > 7.5 mg/day for more than 6 months), excess thyroxine, anticonvulsants
- Ongoing disease conditions e.g. hypogonadism, hyperthyroidism, hyperparathyroidism, Cushing's syndrome, chronic obstructive airways disease, liver disease, malabsorption, chronic renal failure, rheumatoid arthritis, organ transplantation and anorexia nervosa
- Prolonged immobilisation, poor health or fragility
- Lifelong low calcium intake (< 500 mg/day among Asians)
- Lack of regular physical activity

For Asian males, there is no validated osteoporosis self-assessment screening tool available as yet. In view of this, the Health Promotion Board (HPB) recommends that the International Osteoporosis Foundation (IOF) One-Minute Risk Test be used as a risk assessment tool for Asian males instead of the OSTA formula after consultation with the Osteoporosis Society of Singapore (OSS).

The IOF One-Minute Risk Test consists of a series of 10 questions which is recommended for use locally and more than 1 'yes' answer to the questions would warrant a medical consult.

The 10 questions are:

1. Are you aged 65 and above?
2. Do you have a family history of hip fractures?
3. Do you have a thin or small body frame?

4. Have you broken a bone after a fall?
5. Do you smoke?
6. Do you consume less than the recommended level of calcium (800mg)?
7. Do you engage in less than 30 min of physical activity daily? (e.g. jogging, brisk walking, dancing, stair climbing)
8. Do you drink more than 2-3 standard drinks of alcohol a day?
9. Have you taken steroid medication for more than 3 months?
10. Has your doctor ever told you that your level of sex hormones (testosterone) is low?

9.2 Category 3 Screening Tests (Not recommended)

- i) Serum calcium
- ii) Erythrocyte sedimentation rate (ESR)
- iii) Serum phosphate

10) Rheumatoid arthritis^{49, 54, 55, 56}

10.1 Category 3 Screening Tests (Not recommended)

- i) Rheumatoid factor

11) Systemic Lupus Erythematosus (SLE)^{49, 57}

11.1 Category 3 Screening Tests (Not recommended)

- i) Anti-Double Stranded DNA Antibody (Anti-DS DNA Ab)
- ii) Anti-nuclear Antibody (ANA)

12) Thyroid disorder (Thyroid abnormality/ Thyroid dysfunction)

12.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Thyroid function test (TFT)

High Risk Groups:

- a) Obese people as defined conventionally by individuals in high-risk weight categories; hypothyroidism may be asymptomatic and yet, obesity accounts for excessive morbidity and mortality (Diabetes Mellitus, Hyperlipidaemia, Metabolic Syndrome, Polycystic Ovarian Syndrome, Ischaemic Heart Disease, Cancers and Obstructive Sleep

Apnoea). Testing can be done just *once* in the workup for a secondary cause of obesity.

- b) Any individual with autoimmune disease as this will predispose to thyroid disorders such as Grave's Disease or Hashimoto's thyroiditis. The individual should be tested annually with thyroid-stimulating hormone (TSH).
- c) Pregnant women who have diabetes mellitus or adrenal disease as they tend to develop goitre during pregnancy and the consequences of mental retardation in the offspring are severe. Thyroid function test (TFT) should be performed once early on during pregnancy.

E) Musculoskeletal Disorders

1) Back pain (Back disorder)⁴⁵

1.1 Category 3 Screening Tests (Not recommended)

- i) MRI Lumbar Spine

2) Neck pain (Neck disorder)^{46, 47, 48}

2.1 Category 3 Screening Tests (Not recommended)

- i) MRI Cervical Spine

F) Obstetric and Gynaecological Conditions

1) Menopause^{29, 30, 31, 32}

1.1 Category 3 Screening Tests (Not recommended)

- i) Serum 5-Dehydroepiandrosterone (DHEA)
- ii) Serum Estradiol (E2)
- iii) Serum Follicle-stimulating hormone (FSH)
- iv) Serum Insulin-growth factor-1 (IGF1)
- v) Serum Progesterone
- vi) Serum Testosterone

2) **Maternal colonisation with Group B Streptococcus (GBS) during pregnancy**^{68, 69}

2.1 **Category 2** Screening Tests (Suitable for individual-level decision)

- i) Vaginal and rectal swab

High Risk Group: All pregnant women between 35 and 37 weeks gestation.

In 2002, the Centres for Disease Control and Prevention (CDC) recommend universal prenatal screening at 35-37 weeks of gestation. This contradicts the Royal College of Obstetricians and Gynaecologists (RCOG) guideline in 2003 which does not recommend universal prenatal screening for GBS carrier. Though universal screening is not recommended by the RCOG, the indications for intrapartum antimicrobial prophylaxis (IAP) as stated in the RCOG guideline are similar to that of the CDC guideline.

G) Vision and Hearing Disorders

1) **Age-related Macular Degeneration (AMD)**⁶³

1.1 **Category 3** Screening Tests (Not recommended)

- i) AMD screen (Amsler Grid Chart)

2) **Diabetic retinopathy**⁷

2.1 **Category 2** Screening Tests (Suitable for individual-level decision)

- i) Retinal Fundal Photography

Recommendation: All patients diagnosed with diabetes require regular visual acuity assessment and eye examinations by trained personnel to screen for diabetic retinopathy. Type 1 diabetic patients should be examined 3-5 years after diagnosis of diabetes, and at least once yearly subsequently. Type 2 diabetic patients should have an ocular assessment at the time of diagnosis and at least once yearly subsequently.

3) **Glaucoma**

3.1 **Category 3** Screening Tests (Not recommended)

- i) Tonometry

4) **Hearing loss in adults (Deafness in adults)**^{5, 42}

4.1 **Category 2** Screening Tests (Suitable for individual-level decision)

- i) Audiometry

High Risk Group: All persons exposed to excessive noise must undergo pre-employment and annual medical examinations which include audiometry

under the Workplace Safety and Health (Medical Examinations) Regulations by Ministry of Manpower.

5) **Hypertensive retinopathy**

5.1 Category 3 Screening Tests (Not recommended)

- i) Retinal Fundal Photography

6) **Vision disorder**⁵

6.1 Category 3 Screening Tests (Not recommended)

- i) Visual acuity and colour vision test

H) Congenital and Paediatric Conditions

1) **Antenatal and foetal abnormalities (Congenital)**^{62, 70}

1.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Screening tests done in pregnancy or antenatal screening tests (eg. FBC, VDRL, HIV, Hepatitis B, urine microscopy as well as obstetric ultrasound foetal anomaly screening)

Recommendation: The above blood tests and urine test are recommended in early pregnancy (preferably during the first antenatal visit) as a once-off test. All women should be offered an obstetric ultrasound before 22 weeks gestation. This will include an ultrasound for foetal morphology and placenta localisation usually at 18-22 weeks gestation.

2) **Down Syndrome**⁶¹

2.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Down Syndrome screening test

Recommendation: All pregnant women, regardless of age, should be considered to be at risk for foetal aneuploidy and should be offered screening for Down Syndrome. All women should be made aware of the availability of screening tests for Down Syndrome and other chromosomal abnormalities.

This should include Nuchal Translucency Screening (NTS) combined with first trimester maternal serum screening (also known as the first trimester combined screening) or NTS combined with second trimester maternal serum testing (also known as step-wise sequential screening).

3) **Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency in neonates**

3.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Cord blood G6PD screening

Recommendation: *All newborns in Singapore are screened for G6PD deficiency using umbilical cord blood.*

4) **Hearing loss in neonates (Deafness in neonates)**⁴³

4.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Audiometry

Recommendation: *All newborns in Singapore are screened for congenital hearing impairment under the “Universal Newborn Hearing Screening” programme.*

Screening is carried out using automated auditory brain-stem response (AABR), transient evoked oto-acoustic emission (TEOAE) or distortion product oto-acoustic emission (DPOAE). It should be completed preferably before hospital discharge, so that diagnosis of congenital hearing impairment can be confirmed before the infant is 3 months old and intervention can begin before the infant is 6 months old. This is in line with recommendations of the Joint Committee on Infant Hearing (JCIH) 2000 of the American Academy of Paediatrics (AAP).

In high-risk groups who have normal hearing screens at birth but remain at risk of progressive or delayed-onset hearing loss, repeat hearing screen is recommended, at up to 6-monthly intervals.

High-risk conditions for progressive or delayed-onset hearing loss

- a. Parental or caregiver concern over hearing or delayed language, speech or development
- b. Family history of permanent childhood hearing loss
- c. Clinical findings associated with syndromes that are known to include sensori-neural or conductive hearing loss
- d. Postnatal infections associated with sensori-neural hearing loss, including bacterial meningitis
- e. *In utero* infection with toxoplasmosis, rubella, cytomegalovirus, herpes or syphilis
- f. Neonatal conditions, specifically hyper-bilirubinaemia requiring exchange transfusion or persistent pulmonary hypertension requiring mechanical ventilation
- g. Syndromes associated with progressive hearing loss, such as neurofibromatosis
- h. Neuro-degenerative conditions (e.g. Hunter syndrome)

- i. Head trauma
- j. Recurrent or persistent otitis media with effusion for at least 3 months

5) **Inborn errors of metabolism in neonates**⁶⁵

5.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Metabolic Screen (Tandem Mass Spectrometry (TMS))

Recommendation: *Under the National Expanded Newborn Screening Programme, all neonates would undergo an additional newborn screening test called the Metabolic Screen. The metabolic screen tests newborn babies for a group of disorders called Inborn Errors of Metabolism (IEM). About 25 to 30 IEMs can be screened for from a blood spot using a novel technology called Tandem Mass Spectrometry (TMS).*

The metabolic screen test using TMS has a high predictive value with a sensitivity of 96%, specificity 99.8% and recall rate 1.5 - 2%. Patients with grossly abnormal screening tests are referred to metabolic specialists for further management. Those with borderline abnormal results are recalled for a repeat screening test.

6) **Primary hypothyroidism in neonates**

6.1 Category 1 Screening Tests (Suitable for population-level screening)

- i) Thyroid Function Test (TFT)

Recommendation: *All newborns in Singapore will get their cord blood tested once for primary hypothyroidism with thyroid-stimulating hormone (TSH). If TSH is abnormal, then free thyroxine (T4) is tested.*

7) **Retinopathy Of Prematurity (ROP)**⁶⁴

7.1 Category 2 Screening Tests (Suitable for individual-level decision)

- i) Indirect ophthalmoscope, eye speculum or scleral indentor

Recommendation: Screening should be carried out for infants with **any one** of the following:

- Birth weight less than 1500 g **or**
- Gestational age less than 32 weeks **or**
- Prolonged oxygen therapy use

Screening Protocol

- Babies born before 27 weeks gestational age (i.e. up to 26 weeks and 6 days) - the first ROP screening examination should be undertaken at 30 to 31 week
- Babies born between 27 and 32 weeks gestational age (i.e. up to 31 weeks and 6 days) - the first ROP screening examination should be undertaken between 4 to 5 weeks (i.e. 28-35 days) postnatal age
- Babies >32 weeks gestational age but with birth weight <1500 grams – the first ROP screening examination should be undertaken between 4 to 5 weeks (i.e. 28-35 days) postnatal age
- Minimum frequencies of screening should be weekly when:
 - the vessels end in zone I or posterior zone II; **or**
 - there is any plus or pre-plus disease **or**
 - there is any stage 3 disease in any zone
- Minimum frequencies of screening should be every 2 weeks:
 - In all other circumstances until the criteria for termination have been reached
- All babies <32 weeks gestational age or birth weight <1500g or have undergone prolonged oxygen therapy should have their first ROP screening examination prior to discharge

Termination of ROP screening

Screening can be stopped when a baby is no longer at risk of sight-threatening ROP. In babies who never develop any ROP, the risk of sight-threatening ROP developing is minimal once the retinal vessels have entered zone III and eye examinations may be stopped when this happens, usually after 36 completed week's postmenstrual age.

In babies developing ROP which does not meet the criteria for treatment, screening can be safely stopped when any of the following characteristics of regression are seen on at least 2 successive examinations:

- Lack of increase in severity
- Partial resolution progressing towards complete resolution
- Change in colour in the ridge from salmon pink to white
- Transgression of vessels through the demarcation line
- Commencement of the process of replacement of active ROP lesions by scar tissue

8) **Thalassemia** ^{1, 21, 22, 23, 25}

8.1 Category 2 Screening Tests (Suitable for individual-level decision)

i) Thalassemia screen

High Risk Groups:

- a) Pregnant women who are from racial and ethnic groups with a high incidence of haemoglobinopathies (e.g., individuals of African, Caribbean, Latin American, Mediterranean, Middle Eastern, or Southeast Asian descent) should be screened, preferably at the first prenatal visit.
- b) Family history of thalassemia

The screening should be done once-off at the first prenatal visit for pregnant women.

The U.S. Preventive Services Task Force (USPSTF) recommends screening for haemoglobinopathies like thalassemia with haemoglobin electrophoresis or other tests of comparable accuracy in pregnant women at the first prenatal visit. This is especially for those who are members of racial and ethnic groups with a high incidence of haemoglobinopathies (e.g., individuals of African, Caribbean, Latin American, Mediterranean, Middle Eastern, or Southeast Asian descent).

I) Miscellaneous

1) **Benign Prostatic Hyperplasia (BPH)**

1.1 Category 3 Screening Tests (Not recommended)

- i) Prostate-Specific Antigen (PSA)
- ii) MRI Prostate

2) **Chronic Obstructive Pulmonary Disease (COPD)** ^{1, 44}

2.1 Category 3 Screening Tests (Not recommended)

- i) Spirometry

3) **Purpose of identification**

The following tests are for the purposes of identification rather than for health reasons.

- i) Blood group
- ii) Rhesus factor

Part II of Report

Categorisation of screening tests by type of tests

- A) General
- B) Blood (Non-tumour markers)
- C) Blood (Tumour markers)
- D) Urine
- E) Stool
- F) Imaging: X-Ray, Ultrasound, CT, MRI
- G) Eye
- H) Special

A) General

No.	Category	Screening Test	Disease	Details (See)
1	1	Blood pressure measurement	Hypertension	D 6.1 (i)
2	1	Body-Mass Index (BMI)	Obesity	D 8.1 (i)
3	1	Waist Circumference	Obesity	D 8.1 (ii)
4	2	Electrocardiography (ECG)	Coronary Heart Disease	B 5.1 (i)
5	3	Body fat measurement	Obesity	D 8.2 (i)

B) Blood (Non-tumour markers)

Category 1 screening tests

No.	Category	Screening Test	Disease	Details (See)
1	1	Fasting blood glucose	Diabetes mellitus	D 2.1 (i)
2	1	Fasting Lipid	Hyperlipidaemia	D 5.1 (i)
3	1	Thyroid Function Test (TFT)	Primary hypothyroidism in neonates	H 6.1 (i)

Category 2 screening tests

No.	Category	Screening Test	Disease	Details (See)
1	2	Apolipoprotein A	Coronary Heart Disease	B 5.1 (iii)
2	2	Full Blood Count (FBC)	Anaemia (Iron deficiency anaemia)	D 1.1 (i)
3	2	Hepatitis B screen	Hepatitis B	C 3.1 (i)
4	2	hs CRP	Coronary Heart Disease	B 5.1 (ii)
5	2	Human Immunodeficiency Virus (HIV) screen	Human Immunodeficiency Virus Infection	C 1.1 (i)
6	2	Kidney function test/ Renal panel	Kidney disorder/ dysfunction	D 7.1 (i)
7	2	Rubella serology	Rubella	C 6.1 (i)
8	2	Thalassemia screen	Thalassemia	H 8.1 (i)
9	2	Thyroid Function Test (TFT)	Thyroid disorder/ dysfunction	D 12.1 (i)
10	2	VDRL	Syphilis	C 7.1 (i)

Category 3 screening tests

No.	Category	Screening Test	Disease	Details (See)
1	3	Anti-DS DNA Ab	Systemic lupus erythematosus (SLE)	D 11.1 (i)
2	3	ANA	Systemic lupus erythematosus (SLE)	D 11.1 (ii)
3	3	Apolipoprotein B	Coronary Heart Disease	B 5.2 (ii)
4	3	Serum calcium	Osteoporosis	D 9.2 (i)
5	3	Serum 5-Dehydroepiandrosterone (DHEA)	Menopause	F 1.1 (i)

No.	Category	Screening Test	Disease	Details (See)
6	3	Erythrocyte sedimentation rate (ESR)	Osteoporosis	D 9.2 (ii)
7	3	Serum Estradiol (E2)	Menopause	F 1.1 (ii)
8	3	Serum Follicle-stimulating hormone (FSH)	Menopause	F 1.1 (iii)
9	3	HbA1c	Diabetes mellitus	D 2.2 (i)
10	3	Hepatitis A screen	Hepatitis A	C 2.1 (i)
11	3	Hepatitis C Screen	Hepatitis C	C 4.1 (i)
12	3	Homocysteine	Coronary Heart Disease	B 5.2 (iii)
13	3	Insulin-growth factor-1 (IGF1)	Menopause	F 1.1 (iv)
14	3	Serum Phosphate	Osteoporosis	D 9.2 (iii)
15	3	Serum Progesterone	Menopause	F 1.1 (v)
16	3	Rheumatoid factor	Rheumatoid arthritis	D 10.1 (i)
17	3	Serum Testosterone	Menopause	F 1.1 (vi)
18	3	Serum uric acid	Coronary Heart Disease	B 5.2 (iv)
			Gout	D 4.1 (i)

For identification purposes

No.	Category	Screening Test	Disease	Details (See)
1	Nil	Blood group	Purpose of identification	I 3 (i)
2	Nil	Rhesus factor	Purpose of identification	I 3 (ii)

C) Blood (Tumour markers)

Category 2 screening tests

No.	Category	Screening Test	Disease	Details (See)
1	2	Alpha-FoetoProtein (AFP)	Liver cancer (HCC)	A 6.1 (i)
2	2	Prostate-Specific Antigen (PSA)	Prostate cancer	A 12.1 (i)
3	2	Tumour marker for nose (EBV-EA-EBNA-1)	Nasopharyngeal carcinoma (NPC)	A 8.1 (i)

Category 3 screening tests

No.	Category	Screening Test	Disease	Details (See)
1	3	CA 125	Ovarian cancer	A 10.1 (i)
2	3	CA 19-9	Pancreatic cancer	A 11.1 (i)
3	3	Carcinoembryonic antigen (CEA)	Colorectal cancer	A 3.3 (i)
4	3	Liver function test (LFT)	Liver cancer (HCC)	A 6.2 (i)
5	3	Prostate-Specific Antigen (PSA)	Benign Prostate Hyperplasia (BPH)	I 1.1 (i)
6	3	Testicular cancer test (e.g. AFP and beta-HCG)	Testicular cancer	A 13.1 (i)
7	3	Tumour marker for breast (e.g. CEA and CA15-3)	Breast cancer	A 1.3 (ii)
8	3	Tumour marker for lung	Lung cancer	A 7.1 (i)

D) Urine

No.	Category	Screening Test	Disease	Details (See)
1	2	Urine Analysis	Kidney Disorder (Kidney dysfunction/abnormality)	D 7.1 (ii)
2	2	Urine Microalbumin/Creatinine Ratio	Diabetic albuminuria/microalbuminuria /nephropathy	D 3.1 (i)

E) Stool

No.	Category	Screening Test	Disease	Details (See)
1	1	Faecal immunochemical test	Colorectal cancer	A 3.1 (i)
2	2	Stool for ova, cyst and parasites	Intestinal parasitic disease	C 5.1 (i)

F) Imaging

i) X-Ray:

No.	Category	Screening Test	Disease	Details (See)
1	1	Mammogram	Breast cancer	A 1.1 (i)
2	2	Bone Mineral Density (BMD) scan	Osteoporosis	D 9.1 (i)
3	2	Chest X-Ray (CXR)	Tuberculosis (TB)	C 8.1 (i)
4	3	Abdominal X-ray (AXR)	Colorectal cancer	A 3.3 (ii)
5	3	Chest X-Ray (CXR)	Lung cancer	A 7.1 (ii)

ii) Ultrasound:

No.	Category	Screening Test	Disease	Details (See)
1	2	Abdominal Ultrasonography	Abdominal Aortic Aneurysm (AAA)	B 1.1 (i)
2	2	Ultrasound Hepatobiliary System (US HBS)	Liver cancer (HCC)	A 6.1 (ii)
3	2	Transvaginal Ultrasound	Ovarian cancer	A 10.1 (i)
4	3	Duplex Ultrasonography	Carotid artery stenosis	B 4.1 (i)
5	3	Ultrasound Breasts	Breast cancer	A 1.3 (i)
6	3	Ultrasound Pelvis	Cervical dysplasia/cervical carcinoma-in-situ/cervical cancer	A 2.2 (i)
			Endometrial cancer	A 4.1 (i)

iii) CT:

No.	Category	Screening Test	Disease	Details (See)
1	2	CT Colonography	Colorectal cancer	A 3.2 (i)
2	2	CT Coronary Calcium Score	Coronary Heart Disease	B 5.1 (iv)
3	3	CT Abdomen	Colorectal cancer	A 3.3 (iii)
4	3	CT Coronary Angiogram	Coronary Heart Disease	B 5.2 (i)
5	3	CT Pelvis	Cervical dysplasia/cervical carcinoma-in-situ/cervical cancer	A 2.2 (ii)
			Endometrial cancer	A 4.1 (ii)
6	3	Spiral CT scan	Lung cancer	A 7.1 (iii)

iv) MRI:

No.	Category	Screening Test	Disease	Details (See)
1	2	MRI Breast	Breast cancer	A 1.2 (ii)
2	2	MRI Brain/MRA	Cerebral aneurysm	B 2.1 (i)
3	3	MRI Brain/MRA	Cerebrovascular disease (Stroke)	B 3.1 (i)
4	3	MRI Cervical Spine	Neck pain (neck disorder)	E 2.1 (i)
5	3	MRI Lumbar Spine	Back pain (back disorder)	E 1.1 (i)
6	3	MRI Prostate	Benign Prostate Hyperplasia (BPH)	I 1.1 (ii)
			Prostate cancer	A 12.2 (i)

G) Eye

No.	Category	Screening Test	Disease	Details (See)
1	2	Indirect ophthalmoscope, eye speculum or scleral indenter	Retinopathy of Prematurity (ROP)	H 7.1 (i)
2	2	Retinal Fundal Photography	Diabetic retinopathy	G 2.1 (i)
3	3	Visual acuity and colour vision	Vision disorder (vision abnormality)	G 6.1 (i)
4	3	AMD screen (Amsler grid chart)	Age-related Macular Degeneration (AMD)	G 1.1 (i)
5	3	Retinal Fundal Photography	Hypertensive retinopathy	G 5.1 (i)
6	3	Tonometry	Glaucoma	G 3.1 (i)

H) Special

Category 1 screening tests

No.	Category	Screening Test	Disease	Details (See)
1	1	Audiometry	Hearing loss in neonates (Deafness in neonates)	H 4.1 (i)
2	1	Colonoscopy	Colorectal cancer	A 3.1 (ii)
3	1	Cord blood G6PD screening	G6PD Deficiency	H 3.1 (i)
4	1	Metabolic Screen (Tandem Mass Spectrometry (TMS))	Inborn Errors of Metabolism (IEM)	H 5.1 (i)
5	1	Pap Smear	Cervical dysplasia/cervical carcinoma-in-situ/cervical cancer	A 2.1 (i)

Category 2 screening tests

No.	Category	Screening Test	Disease	Details (See)
1	2	Ankle Brachial Index (ABI)	Peripheral vascular disease	B 6.1 (i)
2	2	Antenatal screening tests or pregnancy screening tests (eg. FBC, VDRL, HIV, Hepatitis B, urine microscopy as well as obstetric ultrasound fetal anomaly screening)	Antenatal and foetal abnormalities (Congenital)	H 1.1 (i)
3	2	Audiometry	Hearing loss in adults (Deafness in adults)	G 4.1 (i)
4	2	Down Syndrome screening test	Down Syndrome	H 2.1 (i)
5	2	Nasoscopy	Nasopharyngeal carcinoma (NPC)	A 8.1 (ii)
6	2	Treadmill Stress Test	Coronary Heart Disease	B 5.1 (v)
7	2	Vaginal and rectal swab	Maternal colonisation with GBS during pregnancy	F 2.1 (i)

Category 3 screening tests

No.	Category	Screening Test	Disease	Details (See)
1	3	Oesophago Gastro Duodenoscopy (OGD)	Gastric cancer	A 5.1 (i)
			Oesophageal cancer	A 9.1 (i)
2	3	Spirometry	Chronic Obstructive Pulmonary Disease (COPD)	I 2.1 (i)

Criteria for Categorisation of Screening Tests

1	Suitable for population-level screening
	<p>The disease condition is an important health problem;</p> <p>Its natural history is well understood;</p> <p>It is recognisable at an early stage;</p> <p>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;</p> <p>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)</p> <p>Recommendations made by trusted expert authorities (e.g. local clinical practice guidelines (CPGs), US Preventive Services Task Force) uniformly support use of screening test;</p> <p>Population-level screening programmes have been implemented successfully elsewhere;</p> <p>Cost-effectiveness data available, based on preferable local, or, if not, overseas data reporting cost effective analysis ratios within the acceptable threshold for Singapore.</p>
2	Suitable for individual-level decision
	<p>The disease is recognisable at an early stage;</p> <p>There is some evidence that use of the screening tests improves survival, though not necessarily at same level of robustness;</p> <p>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;</p> <p>Risk-benefit ratio of benefit to harm is different for different individuals, and may exceed 1 in some groups;</p> <p>Cost-effectiveness data suggest cost effective analysis ratios are above acceptable threshold for Singapore, or there is no cost-effectiveness data.</p>
3	Not recommended
	<p>The current evidence is insufficient to assess the balance of benefits and harms of the service;</p> <p>Evidence is lacking, or of poor quality, or is conflicting so that no decision can be</p>

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

US Preventive Services Taskforce Recommendation Categories Compared to the Proposed 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.	Refer to 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”

List of Category 1 Screening Tests

No.	Screening Test	Disease	Age Group
1	Audiometry	Hearing loss in neonates	All neonates
2	Blood pressure measurement	Hypertension	Individuals aged 18 yrs and above
3	Body Mass Index (BMI)	Obesity	Individuals aged 18 yrs and above
4	Colonoscopy ¹	Colorectal cancer	Individuals aged 50 yrs and above
5	Faecal immunochemical test ² (FIT)	Colorectal cancer	Individuals aged 50 yrs and above
6	Fasting blood glucose	Diabetes Mellitus	Individuals aged 40 yrs and above
7	Fasting Lipid	Hyperlipidaemia	Individuals aged 40 yrs and above
8	G6PD screen with cord blood	G6PD deficiency in neonates	All neonates
9	Mammogram	Breast cancer	Women aged 50-69 yrs
10	Metabolic Screen (Tandem Mass Spectrometry (TMS))	Inborn Errors of Metabolism (IEM)	All neonates
11	Pap smear	Cervical cancer	Women aged 25-69 yrs
12	Thyroid Function Test (TFT)	Primary hypothyroidism in neonates	All neonates
13	Waist Circumference	Obesity	Individuals aged 18 yrs and above

^{1,2} Either an annual FIT or a 10-yearly colonoscopy is recommended for colorectal cancer screening in an average-risk individual aged 50 years and above.

List of Category 2 Screening Tests

No.	Screening Test	Disease	High Risk Group
1	Abdominal Ultrasonography	Abdominal Aortic Aneurysm (AAA)	Men aged 65 to 75 who have ever smoked
2	Alpha-FoetoProtein (AFP)	Liver cancer (HCC)	Hepatitis B carrier or individuals with liver cirrhosis
3	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
4	Antenatal and pregnancy screening tests	Antenatal and foetal abnormalities (Congenital)	All pregnant women
5	Apolipoprotein A	Coronary Heart Disease	Individuals with intermediate coronary heart disease risk
6	Audiometry	Hearing loss in Adults	Individuals exposed to excessive noise
7	Bone mineral density scan (BMD)	Osteoporosis	Individuals with high osteoporosis risk e.g. high OSTA score
8	Chest X-ray (CXR)	Tuberculosis (TB)	Close contacts of TB or foreigners from countries with high disease prevalence
9	CT Colonography	Colorectal cancer	Individuals above 50 yrs not going for screening colonoscopy or FIT
10	CT Coronary Calcium Score	Coronary Heart Disease	Individuals with intermediate coronary heart disease risk
11	Down Syndrome screening test	Down Syndrome	All pregnant women
12	ECG	Coronary Heart Disease	Individuals with intermediate coronary heart disease risk
13	Full Blood Count (FBC)	Anaemia (Iron-deficiency anaemia)	All pregnant women, women of childbearing age, high risk infants, high risk children

14	Hepatitis B screen	Hepatitis B infection	All pregnant women, immigrants from countries where Hepatitis B are endemic
15	hs CRP	Coronary Heart Disease	Individuals with intermediate coronary heart disease risk
16	Human Immunodeficiency Virus (HIV) screen	Human Immunodeficiency Virus Infection	All pregnant women, individuals with high-risk sexual behaviour, intravenous drug abusers, individuals who had blood transfusion
17	Kidney function test	Kidney disorder/ dysfunction	Individuals with diabetes mellitus or hypertension or cardiovascular disease, individual aged 50 yrs and above who is a smoker, individuals with family history of end-stage renal failure
18	MRI/ MRA brain	Cerebral aneurysm	Individuals with personal or family history of aneurysmal subarachnoid haemorrhage, individuals with autosomal dominant polycystic kidney disease
19	MRI Breast	Breast cancer	Proven BRCA carriers, women at high genetic risk for breast cancer
20	Nasoscopy	Nasopharyngeal carcinoma (NPC)	Individuals with a first degree relative with NPC, individuals with 2 or more relatives with NPC
21	Prostate-Specific Antigen (PSA)	Prostate cancer	Men aged 50-75 yrs, high-risk men such as men with a strong family history of prostate cancer
22	Retinal Fundal Photography	Diabetic retinopathy	All individuals with diabetes mellitus
23	ROP screen	Retinopathy of prematurity (ROP)	Infants with birth weight <1500g or gestational age < 32 wks or prolonged oxygen therapy use
24	Rubella serology	Rubella	All pregnant women
25	Stool for ova, cyst and parasites	Intestinal parasitic infection	Immigrants from countries with high disease prevalence
26	Thalassemia screen	Thalassemia	Pregnant women from ethnic groups with high disease

			prevalence or individuals with family history of disease
27	Thyroid function test (TFT)	Thyroid disorder	Obese individuals, individuals with autoimmune disease, pregnant women with diabetes mellitus or adrenal disease
28	Transvaginal Ultrasound	Ovarian Cancer	BRCA carriers
29	Treadmill Stress Test	Coronary Heart Disease	Individuals with intermediate coronary heart disease risk
30	Tumour marker for NPC	Nasopharyngeal carcinoma (NPC)	Individuals with a first degree relative with NPC, individuals with 2 or more relatives with NPC
31	Ultrasound Hepatobiliary System	Liver cancer (HCC)	Hepatitis B carrier or individuals with liver cirrhosis
32	Urine analysis	Kidney disorder/dysfunction	Individuals with diabetes mellitus or hypertension or cardiovascular disease, individual aged 50 yrs and above who is a smoker, individuals with family history of end-stage renal failure
33	Urine microalbumin/creatinine ratio	Diabetic albuminuria/nephropathy	All individuals with diabetes mellitus
34	Vaginal and rectal swab	Maternal colonisation with GBS during pregnancy	All pregnant women between 35 and 37 weeks gestation.
35	VDRL	Syphilis	All pregnant women, individuals with high-risk sexual behaviour, intravenous drug abusers

References:

- 1) The US Preventive Services Task Force
Website: <http://www.ahrq.gov/clinic/cps3dix.htm>
- 2) Ministry of Health (MOH) Clinical Practice Guidelines (CPG) website
Website: <http://www.moh.gov.sg/mohcorp/publications.aspx?id=16266>
- 3) MOH CPG on obesity
- 4) MOH CPG on health screening
- 5) MOH CPG on functional screening
- 6) MOH CPG on lipids
- 7) MOH CPG on diabetes mellitus
- 8) MOH CPG on cancer screening
- 9) MOH CPG on glomerulonephritis
- 10) MOH CPG on screening for cardiovascular disease and risk factors (Draft)
- 11) MOH CPG for use of ECG for screening of coronary heart disease in asymptomatic patients with hypertension
- 12) MOH CPG on osteoporosis
- 13) The Centres for Disease Control and Prevention (CDC)
Website: <http://www.cdc.gov>
- 14) CDC morbidity and mortality report on Recommendations to Prevent and Control Iron Deficiency in the United States (April 3, 1998 / Vol. 47 / No. RR-3)
- 15) American Diabetes Association 2010 Clinical Practice Recommendations
Website: http://care.diabetesjournals.org/content/33/Supplement_1
- 16) WHO report on definition and diagnosis of DM and intermediate hyperglycaemia
Website: www.who.int/.../Definition%20and%20diagnosis%20of%20diabetes_new.pdf
- 17) CDC (Centre for Disease Control and Prevention) - Yellow Book: Chapter 4
Website: <http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-4/asymptomatic-screening.aspx>
- 18) American Association of Family Physician- Hepatitis A (*Am Fam Physician*. 2006 Jun 15; 73(12):2162-2168)
Website: <http://www.aafp.org/afp/2006/0615/p2162.html>

- 19) Clinical Infectious Diseases 2005; 41:e86–e88 © 2005 by the Infectious Diseases Society of America. DOI: 10.1086/497073 Detection of Immunoglobulin M Antibody to Hepatitis A Virus in Alaska Residents without Other Evidence of Hepatitis
Website: <http://www.journals.uchicago.edu/doi/full/10.1086/497073>
- 20) US Preventive Services Task Force and CDC (Centre for Disease Control and Prevention) joint recommendation on evidence statement:

Healthy pregnancy (Screening, Testing, Counselling, Immunization, and Preventive Medication) and Rubella (Screening)

Website: www.businessgrouphealth.org/.../topics/.../rhd_pregnancy_es.pdf
- 21) Guide to Clinical Preventive Service, US Preventive Services Task Force

Screening for Hemoglobinopathies

Website: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hscps2ed1996&part=A14557>
- 22) British Journal of Haematology article on significant haemoglobinopathies: guidelines for screening and diagnosis Volume 149, Issue 1, Pages 35-49

Website: <http://www3.interscience.wiley.com/cgi-bin/fulltext/123239018/HTMLSTART?CRETRY=1&SRETRY=0>
- 23) Clinical practice guideline by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists (CCMG) on Carrier Screening for Thalassemia and Hemoglobinopathies in Canada (No. 218, October 2008)

Website: www.sogc.org/guidelines/documents/gui218CPG0810.pdf
- 24) National Guidelines Clearinghouse

Website: http://www.guideline.gov/summary/summary.aspx?doc_id=13350

Website: http://www.guideline.gov/summary/summary.aspx?doc_id=10920#s23
- 25) American College of Obstetricians and Gynecologists (ACOG). Hemoglobinopathies in pregnancy. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2007 Jan. 9 p. (ACOG practice bulletin; no. 78).

Website: http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=10920&nbr=5700
- 26) American College of Radiology guideline on US pelvis

Website: http://www.acr.org/.../quality_safety/guidelines/us/us_pelvic.aspx
- 27) National Guideline Clearinghouse on pelvic inflammatory disease. Sexually transmitted diseases treatment guidelines 2006.

Website: www.guideline.gov/summary/summary.aspx?doc
- 28) E-medicine article: Author: Shikha Mudgil, MD, Consulting Staff, Department of Radiology, Riddle Memorial Hospital, Aug 10, 2009

Website: <http://emedicine.medscape.com/article/404537-overview>

- 29) Which is the best way to diagnose menopause?
Journal of Family Practice, Nov, 2005 by Leila C. Kahwati, Lori Haigler, Stacy Rideout
Website: www.jfponline.com/pdf%2F5411%2F5411JFP_ClinicalInquiries6.pdf
- 30) Australasian Menopause Society
Website:
http://www.menopause.org.au/index2.php?option=com_content&task=emailform&id=420
- 31) Pub Med, N Z Med J. 1996 May 10; 109(1021):156-9, article on IGF-1 and IGFBP-3 screening for disorders of growth hormone secretion
Website: <http://www.ncbi.nlm.nih.gov/pubmed/8657365>
- 32) American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Menopause:
Website: www.aace.com/pub/pdf/guidelines/menopause.pdf - United States
- 33) SIGN (Scottish Intercollegiate Guidelines Network) on management of oesophageal and gastric cancer, a national clinical guideline
Website: www.sign.ac.uk/pdf/sign87.pdf
- 34) American College of Radiology practice guidelines for the performance of abdominal radiography
Website: www.acr.org/.../quality_safety/guidelines/.../abdominal_radiography.aspx
- 35) American College of Radiology practice guidelines for the performance of CT abdomen and CT pelvis
Website: www.acr.org/.../quality_safety/guidelines/.../ct_abdomen_pelvis.aspx
- 36) Pub Med, paper on multiparametric MRI for prostate cancer screening, Ned Tijdschr Geneeskd. 2009; 153:B487
Website: www.ncbi.nlm.nih.gov/pubmed/20003566
- 37) Oxford journal on the review of uric acid and cardiovascular disease risk (Q J Med 2000; 93: 707-713 © 2000) and the Annals of Internal Medicine by American College of Physicians
Website: qjmed.oxfordjournals.org/cgi/content/full/93/11/707
- 38) Serum Uric Acid and Coronary Heart Disease in 9,458 Incident Cases and 155,084 Controls: Prospective Study and Meta-Analysis, (10.1371/journal.pmed.0020076)
Website:
<http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.0020076>
- 39) Annals of Internal Medicine by American College of Physicians: Serum Uric Acid and Risk for Cardiovascular Disease and Death: The Framingham Heart Study (Ann Intern Med. 1999; 131:7-13. Annals of Internal Medicine · Volume 131 · Number 1)
Website: www.annals.org/content/131/1/7.full.pdf

- 40) National Guideline Clearinghouse: Institute for Clinical Systems Improvement (ICSI) on Hypertension diagnosis and treatment
 Website: http://www.guideline.gov/summary/summary.aspx?doc_id=13481&nbr=006890&string=hypertension
- 41) WHO clinical guidelines for the management of hypertension
 Website: http://www.emro.who.int/publications/Book_Details.asp?ID=191
- 42) MOM Guidelines on Hearing Conservation Programme (HCP)
 Website: www.mom.gov.sg/.../Guidelines%20on%20Hearing%20Conservation%20Programme.pdf
- 43) Universal Newborn Hearing Screening- The need, implementation and challenges
 Website: www.annals.edu.sg/pdf/34VolNo4200505/V34N4p301.pdf
- 44) Global Initiative for Chronic Obstructive Lung Disease
 Website: <http://www.goldcopd.com/guidelinesresources.asp?l1=2&l2=0>
- 45) National Guideline Clearinghouse
 Diagnosis and treatment of low back pain: A joint clinical practice guideline from the American College of Physicians and the American Pain Society
 Website: http://www.guideline.gov/summary/summary.aspx?doc_id=11515
- 46) AAFP (American Association of Family Physician) Cervical Radiculopathy: Nonoperative Management of Neck Pain and Radicular Symptoms
 JASON DAVID EUBANKS, MD, *Case Western Reserve University School of Medicine, Cleveland, Ohio*
 Website: <http://www.aafp.org/afp/2010/0101/p33.html>
- 47) AAFP (American Association of Family Physician) Cervical Spondylotic Myelopathy: A Common Cause of Spinal Cord Dysfunction in Older Persons
 WILLIAM F. YOUNG, M.D., Temple University Hospital, Philadelphia, Pennsylvania
 Website: <http://www.aafp.org/afp/20000901/1064.html>
- 48) American College of Radiology guidelines on chronic neck pain
 Website: www.acr.org/.../quality_safety/app_criteria/.../chronicNeckpainDoc9.aspx
- 49) American College of Rheumatology
 Website: <http://www.rheumatology.org/>
- 50) E-medicine website
 Gout: Differential Diagnoses & Workup, Author: Anne V Miller, MD, Assistant Professor of Medicine, Division of Rheumatology, Southern Illinois University School of Medicine

- Website: <http://emedicine.medscape.com/article/329958-diagnosis>
- 51) American Association of Family Physicians: Gout: An update
AARON T. EGGEBEEN, MD, University of Pittsburgh Arthritis Institute, Pittsburgh, Pennsylvania *Am Fam Physician*. 2007 Sep 15; 76(6):801-808.
Website: <http://www.aafp.org/afp/2007/0915/p801.html>
- 52) *Annals of the Rheumatic Disease*. 2006 October; 65(10): 1301–1311.
Published online 2006 June 2. doi: 10.1136/ard.2006.055251.
EULAR evidence based recommendations for gout. Part I: Diagnosis. Report of a task force of the standing committee for international clinical studies including therapeutics (ESCIIT)
Website: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1798330/?tool=pubmed>
- 53) American College of Obstetricians and Gynecologists
Website: www.acog.org/
- 54) NICE, National Institute for Health and Clinical Excellence on Rheumatoid arthritis
Website: <http://www.nice.org.uk/guidance/index.jsp?action=byTopic&o=8485&ht=7299>
- 55) Scottish Intecollegiate Guidelines Network on management of early rheumatoid arthritis
Website: <http://www.sign.ac.uk/guidelines/fulltext/48/index.html>
- 56) American association of family physician article on diagnosis and management of rheumatoid arthritis J. ADAM RINDFLEISCH, M.D., and DANIEL MULLER, M.D., PH.D. *University of Wisconsin–Madison, Madison, Wisconsin Am Fam Physician*. 2005 Sep 15; 72(6):1037-1047.
Website: <http://www.aafp.org/afp/2005/0915/p1037.html>
- 57) American association of family physician article on diagnosis of Systemic Lupus Erythematosus *Am Fam Physician*. 2003 Dec 1; 68(11):2179-2187.
Website: <http://www.aafp.org/afp/2003/1201/p2179.html>
- 58) American association of family physician article on intracranial aneurysms: current evidence and clinical practice. *Am Fam Physician*. 2002 Aug 15; 66(4):601-609.
Website: <http://www.aafp.org/afp/2002/0815/p601.html>
- 59) Article on chronic kidney disease awareness, screening and prevention: rationale for the design of a public education program. *Nephrology (Carlton)* 2010 Jun;15 Supple 2:37-42
Website: <http://www.ncbi.nlm.nih.gov/pubmed/20586946>
- 60) National Kidney Foundation: Kidney Early Evaluation Program (KEEP)
Website: <http://www.kidney.org/news/keep/index.cfm>

- 61) College of Obstetricians and Gynaecologists, Singapore, guidelines on recommended best practice on antenatal screening for Down Syndrome and other fetal aneuploidies January 2008
Website: http://www.ams.edu.sg/chapter/cogs/Consensus_Statement_Downs_Syndrome.pdf
- 62) The Royal Australian and New Zealand College of Obstetricians and Gynaecologists statement on pre-pregnancy counselling and routine antenatal assessment in the absence of pregnancy complications.
Website: <http://www.ranzcog.edu.au/publications/statements/C-obs3.pdf>
- 63) American Academy of Ophthalmology Preferred Practice Patterns for Age-Related Macular Degeneration
Website: http://one.aao.org/CE/PracticeGuidelines/PPP_Content.aspx?cid=f413917a-8623-4746-b441-f817265eafb4
- 64) The Royal College of Ophthalmologists on UK Retinopathy of Prematurity Guideline May 2008
Website:
http://www.rcophth.ac.uk/docs/scientific/Guideline_Retinopathy_of_Prematurity_2008.pdf
- 65) Article on Expanded Newborn Screening Using Tandem Mass Spectrometry
Website:
<http://www.singhealth.com.sg/DoctorsAndHealthcareProfessionals/MedicalArticles/Aescapulus/2007/Pages/Expanded-Newborn-Screening-Using-Tandem-Mass-Spectrometry.aspx>
- 66) Article on Pattern and Outcome of Subsidised Referrals to Cardiology Specialist Outpatient Clinics (Kwok et al. Ann Acad Med Singapore 2008; 37:103-8)
Website: <http://www.annals.edu.sg/pdf/37VolNo2Feb2008/V37N2p103.pdf>
- 67) Article on Aspirin for prevention of cardiovascular events in a general population screened for a low ankle brachial index: a randomized controlled trial. JAMA. 2010 Mar 3;303(9):841-8.
Website: <http://jama.ama-assn.org/cgi/content/full/303/9/841>
- 68) CDC guidelines on Prevention of Perinatal Group B Streptococcal Disease
Website: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5111a1.htm>
- 69) Royal College of Obstetricians and Gynaecologists (RCOG) guidelines on Prevention of early onset neonatal Group B streptococcal disease
Website: <http://www.rcog.org.uk/womens-health/clinical-guidance/preventing-group-b-streptococcus-gbs-infection-newborn-babies>
- 70) International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) Prenatal Ultrasound Screening Task Force Practice Guidelines for performance of the routine mid-trimester foetal ultrasound scan
Website: http://www.isuog.org/NR/ronlyres/66695A04-5937-4EAB-AA90-E01E7E9D9A33/0/ISUOG_PrenatalUS_Guidelines_externalreview.pdf
- 71) International Osteoporosis Foundation

Website: <http://www.iofbonehealth.org/>

- 72) Screening for osteoporosis in men: a clinical practice guideline from the American College of Physicians

Website: <http://www.annals.org/content/148/9/680.full>

Acknowledgment

The Committee would like to express its sincere thanks to the various Chapters and Colleges of the Academy of Medicine, Singapore and the College of Family Physicians Singapore, for their valuable inputs and contributions to the report.