MINISTRY OF HEALTH
SINGAPORE

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All Registered Medical Practitioners

RELEASE OF NEW SCREENING TEST REVIEW COMMITTEE GUIDELINES, INCLUDING CHANGES TO DIABETES MELLITUS, LIPID DISORDERS, AND CERVICAL CANCER SCREENING

1. The Screening Test Review Committee (STRC), under the Academy of Medicine Singapore (AMS), reviews and makes recommendations on the appropriate use of specific screening tests based on prevailing scientific evidence. The STRC Guidelines 2019, updated from the previous version in 2011, has been published on the AMS website and can be found at [https://www.ams.edu.sg/policy-advocacy/public-policy-resources].

2. Under the guidelines, screening tests have been classified into three categories to guide medical professionals who provide screening for their patients:

(i) Category 1 – Suitable for population-level screening (i.e. Good and robust evidence that the test is both clinically effective and cost effective for screening of the general population).

(ii) Category 2 – Suitable for individual-level decision (i.e. Screening may be useful for high-risk populations, or there is evidence that the test is clinically effective but cost-effectiveness has not been evaluated or is not favourable).

(iii) Category 3 – Not recommended (i.e. There is insufficient evidence to make a decision regarding the usefulness of the test, or there is good evidence that the test is not cost-effective, or that the net harms outweigh benefits).

The list of recommended Category 1 and 2 tests can be found in Annex A and B.

3. The Ministry of Health (MOH) has also introduced changes to population-level screening recommendations in Singapore based on a review of local and international evidence, and the endorsement of relevant professional bodies, including the STRC. The changes are as follows:

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(i) Use of HbA1c as an alternative screening test for diabetes mellitus (in addition to Fasting Plasma Glucose, which remains one of the recommended tests) (See Annex C for details).

(ii) Use of non-fasting lipid profile as an alternative initial screening test for lipid disorders (in addition to fasting lipid profile, which remains one of the recommended tests) (See Annex D for details).

(iii) Use of the Human Papillomavirus (HPV) test as the new primary screening test (instead of Pap smear) for cervical cancer, for women aged 30 years and above (See Annex E for details).

The alternate screening tests for diabetes mellitus and lipid disorders could facilitate opportunistic screening. The new HPV test for cervical cancer screening has better sensitivity and reduces frequency of screening for women aged 30 years and above.

4. Recommendations reflected in this circular are effective immediately. However, under the Screen for Life (SFL) Programme, subsidies for the above mentioned tests will only be available from 7 May 2019 onwards. For Community Health Assist Scheme (CHAS) General Practitioners (GP), you will also receive a separate circular which will provide more details on the corresponding operational changes to the SFL programme, in view of the revised population-level screening recommendations as detailed in para 2.

5. Please email MOH_INFO@moh.gov.sg, should you require further clarifications.

Thank you.

A/PROF BENJAMIN ONG
DIRECTOR OF MEDICAL SERVICES
MINISTRY OF HEALTH

ANNEX A

LIST OF CATEGORY 1 SCREENING TESTS[1]

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[2]	Colorectal cancer	Individuals aged 50 yrs and above
5	Faecal Immunochemical Test[3] (FIT)	Colorectal cancer	Individuals aged 50 yrs and above
6	Fasting blood glucose	Diabetes Mellitus	Individuals aged 40 yrs and above
7	Glycated Haemoglobin (HbA1c)	Diabetes Mellitus	Individuals aged 40 yrs and above
8	Fasting Lipids	Hyperlipidaemia	Individuals aged 40 yrs and above
9	Non-fasting Lipids	Hyperlipidaemia	Individuals aged 40 yrs and above
10	G6PD screen with cord blood	G6PD deficiency in neonates	All neonates
11	Human Papillomavirus (HPV) DNA test	Cervical dysplasia/ cervical intraepithelial lesion /cervical cancer	Women aged 30 years and above who ever had sexual intercourse
12	Mammogram	Breast cancer	Women aged 50-69 yrs
13	Metabolic Screen (Tandem Mass Spectrometry (TMS))	Inborn Errors of Metabolism (IEM)	All neonates
14	Pap Smear	Cervical dysplasia/ cervical intraepithelial lesion /cervical cancer	Women aged 25 to 29 years who ever had sexual intercourse
15	Spinal screening (Scoliometer)	Scoliosis	All individuals during the early adolescent years
16	Thyroid Function Test (TFT)	Primary hypothyroidism in neonates	All neonates
17	Vision acuity test	Developmental vision disorder (in children)	Children aged 3 years and above
18	Waist Circumference	Obesity	Individuals aged 18 yrs and above

[1] Category 1 screening tests are suitable for population-level screening; there is good and robust evidence that these tests are clinically effective and cost effective for use at the population level.
[2,3] 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.

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ANNEX B

LIST OF CATEGORY 2 SCREENING TESTS[4]

No.	Screening Test	Disease	High Risk Group
1.	Abdominal Ultrasonography	Abdominal Aortic Aneurysm	Men aged 65 to 75 who have ever smoked
2.	Alpha-Fetoprotein	Liver cancer	Hepatitis B carrier or individuals with liver cirrhosis
3.	Ankle Brachial Index	Peripheral vascular disease	Individuals with diabetes mellitus; Individuals aged 50-70 yrs and are smokers or with both hypertension and hyperlipidaemia
4.	Antenatal and pregnancy screening tests	Antenatal and foetal abnormalities (Congenital)	All pregnant women
5.	Apolipoprotein A and B	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	Osteoporosis	Individuals with high osteoporosis risk e.g. high OSTA score
8.	Chest X-ray	Tuberculosis (TB)	Close Contacts; 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	Down Syndrome	All pregnant women
12.	Electrocardiography	Coronary Heart Disease	Individuals with intermediate coronary heart disease risk
13.	Faecal Immunochemical Test (FIT) – DNA test	Colorectal cancer	Individuals aged 50 yrs and above
14.	Full Blood Count	Anaemia (Iron-deficiency)	All pregnant women, women of childbearing age, high risk infants, high risk children
15.	Hepatitis B screen	Hepatitis B infection	All pregnant women; Asymptomatic Singapore residents with no known hepatitis B carrier status and have not been previously vaccinated; Healthcare workers;

[4] Category 2 screening tests are suitable for individual-level decisions; the screening tests may be useful for high-risk populations, or there is evidence that the screening tests are effective, but favourable cost-effectiveness has not been established.

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No.	Screening Test	Disease	High Risk Group
			Immigrants from countries where Hepatitis B is endemic; Individuals with known exposure to HBV; Individuals on chronic hemodialysis; Intravenous drug abusers; Individuals who have undergone invasive procedures in healthcare facilities with inadequate infection control practices; Individuals with HBV-positive or at-risk sex partners; HIV patients
16.	Hepatitis C screen	Hepatitis C infection	Children born to HCV-positive mothers; Individuals with known exposure to HCV; Individuals on chronic hemodialysis; Intravenous drug abusers; Individuals who have undergone invasive procedures in healthcare facilities with inadequate infection control practices; Individuals with HCV-positive or at-risk sex partners; Healthcare workers; HIV patients
17.	hsCRP	Coronary Heart Disease	Individuals with intermediate coronary heart disease risk
18.	Human Immunodeficiency Virus (HIV) screen	Human Immunodeficiency Virus Infection	All pregnant women; Healthcare workers; Individuals with active TB infection; Individuals with at-risk sexual behaviour; Intravenous drug abusers, Individuals with HIV-positive or at-risk sex partners; Individuals with known HIV exposure
19.	Interferon-gamma release assay	Tuberculosis (TB)	Close contacts of TB; High-risk individuals: HIV, patients receiving anti-TNF agents, dialysis, transplants (solid organ and haematological)
20.	Kidney function test	Kidney disorder/ dysfunction	Individuals with diabetes mellitus or hypertension or cardiovascular disease; Individuals aged 50 yrs and above who are smokers; Individuals with a family history of end-stage renal failure
21.	Low-dose CT screening	Lung cancer	Individuals aged between 55-74 who have smoked ≥ 30 pack years and are continuing to smoke; Individuals aged between 55-74 who have smoked ≥ 30 pack years but quit <15 years ago
22.	MRI/ MRA brain	Cerebral aneurysm	Individuals with a personal or family history of 2 or more first-degree relatives with subarachnoid haemorrhage; Individuals with autosomal dominant polycystic kidney disease
23.	MRI Breast	Breast cancer	Proven BRCA carriers; Women at high genetic risk for breast cancer; Women with breast injection augmentation that severely impairs evaluation of the breasts on mammography and sonography
24.	Nasopharyngoscopy	Nasopharyngeal carcinoma	Individuals with a first degree relative with Nasopharyngeal carcinoma
25.	Oesophago- gastro Duodenoscopy	Gastric cancer	Individuals with Hereditary Non-Polyposis Colon cancer or Lynch Syndrome
26.	Pelvis X-ray (Antero-posterior)	Spastic hip displacement	Children with cerebral palsy
27.	Prostate-Specific Antigen (PSA)	Prostate cancer	Men aged 50-70 yrs; High-risk men such as men with a strong family history of prostate cancer may be offered screening at an earlier age
28.	Retinal Fundal Photography	Diabetic retinopathy	All individuals with diabetes mellitus
29.	ROP screen	Retinopathy of prematurity	Infants with birth weight <1500g; Gestational age < 32 wks; Prolonged oxygen use

No.	Screening Test	Disease	High Risk Group
30.	Rubella serology	Rubella	All pregnant women
31.	Stool for ova, cyst and parasites	Intestinal parasitic infection	Immigrants from countries with high disease prevalence
32.	Syphilis Enzyme Immunoassay (EIA)	Syphilis	All pregnant women; Individuals with at-risk sexual behavior; HIV patients
33.	Thalassemia screen	Thalassemia	Pregnant women from ethnic groups with high disease prevalence; Individuals with a family history of Thalassemia
34.	Thyroid Function Test (TFT)	Thyroid disorder	Obese individuals; Individuals with autoimmune disease; Pregnant women with diabetes mellitus or adrenal disease
35.	Transvaginal Ultrasound	Ovarian cancer	BRCA carriers
36.	Treponema Pallidium Particle Agglutination / Treponema Pallidum Haemagglutination	Syphilis	All pregnant women; Individuals with at-risk sexual behaviour
37.	Treadmill Stress Test	Coronary Heart Disease	Individuals with an intermediate coronary heart disease risk
38.	Tuberculin Skin Test	Tuberculosis	Close contacts of TB
39.	Tumour marker for NPC (EBV-EA-EBNA-1)	Nasopharyngeal Carcinoma (NPC)	Individuals with a first degree relative with NPC
40.	Ultrasound Hepatobiliary System	Liver cancer	Hepatitis B carriers; Individuals with liver cirrhosis
41.	Ultrasound pelvis	Endometrial cancer	Individuals with Hereditary non-polyposis Colon cancer or Lynch syndrome
42.	Urine analysis	Kidney disorder/ dysfunction	Individuals with diabetes mellitus or hypertension or cardiovascular disease; Individuals aged 50 yrs and above who are smokers; Individuals with a family history of end-stage renal failure
43.	Urine or cervical/urethral swab for PCR	Chlamydia and Gonorrohea	Individuals with at-risk sexual behaviour
44.	Urine microalbumin/ creatinine ratio	Diabetic albuminuria/ nephropathy	All individuals with diabetes mellitus
45.	Vaginal and rectal swab	Maternal colonisation with GBS in pregnancy	All pregnant women between 35 and 37 weeks gestation.

ANNEX C

USE OF HBA1C AS AN ALTERNATIVE INITIAL SCREENING TEST FOR DIABETES MELLITUS

1. All doctors should note that **HbA1c may be used an alternative initial screening test for Diabetes Mellitus (DM)**. This is in line with international guidelines adopted by the World Health Organization (WHO), the International Expert Committee of the American Diabetes Association (ADA), as well as other countries such as Australia, New Zealand, Japan and Malaysia.

2. Based on analyses of the 2010 National Health Survey data, HbA1c results of 6.0% and below correlated well with a diagnosis of No Diabetes, while HbA1c of 7.0% and above correlated well with a diagnosis of Diabetes. A screening HbA1c result of between 6.1% and 6.9% would necessitate further tests with either a Fasting Plasma Glucose (FPG) or a 2-hour Oral Glucose Tolerance Test (2hOGTT) (Table 1).

Table 1: Summary of HbA1c Screening Guidelines

	HbA1c screening	**Interpretation**	**Action**	**Recommended Diagnosis**
High risk of DM^ **OR** **Age ≥40 years**	6.0% and below	Low probability of diabetes.	No further tests needed if there are no symptoms of diabetes[5]. Further testing with an FPG or a 2hOGTT is recommended in the presence of clinical suspicion of diabetes.	**No Diabetes** Maintain healthy lifestyle and weight. Repeat test in 3 years.
	6.1% to 6.9%	Proceed to FPG or OGTT.	FPG ≤ 6.0mmol/L OR 2hOGTT< 7.8 mmol/L	
			FPG 6.1 - 6.9 mmol/L OR 2hOGTT 7.8 - 11.0 mmol/L	**Pre-diabetes** Manage as per Appropriate Care Guidelines (ACG).
			FPG ≥ 7.0 mmol/L OR 2hOGTT ≥ 11.1 mmol/L	**Diabetes** Manage accordingly.
	7.0% and above	High probability of diabetes.	No further tests needed.	

^ Risk factors include: overweight/obesity (BMI ≥ 25.0 kg/m^2); first degree relative with DM; high risk ethnicity; women who have delivered a baby 4kg or more, or with previous gestational DM; hypertension; low HDL cholesterol or high triglyceride level; women with polycystic ovarian syndrome; impaired glucose tolerance or impaired fasting glucose; or individuals identified to be at high risk via the diabetes risk assessment tool.

[5] Symptoms of diabetes mellitus include: frequent urination, increased thirst, weight loss with no obvious cause, frequent skin infections, slow wound healing, and blurring of vision. Of note, these symptoms are not specific for diabetes.

3. In using HbA1c as a screening test for diabetes, doctors should be aware of certain medical conditions and physiological states that may affect the accuracy of the HbA1c measurement. In the presence of these conditions, the use of HbA1c for screening of diabetes is not recommended. These include:

a. Haemoglobinopathies. The presence of haemoglobinopathies (thalassaemia[6] or variant haemoglobin traits) can interfere with HbA1c laboratory methods, causing spuriously high or low results.

b. Other medical conditions. As HbA1c measures the level of glycated haemoglobin over the past 6-12 weeks, any condition that leads to an increase or decrease in turnover of red blood cells would lead to spurious results (Table 2).

Table 2: Conditions that may lead to spurious HbA1c results

Condition	Physiological effects	Effect on HbA1c
Haemoglobinopathies (e.g. thalassaemia and haemoglobin variant)	Shortened red blood cell lifespan. Additionally, they may interfere with certain laboratory methods. These interfering effects are variable, depending on the method used.	Decreased
Iron deficiency anaemia	Prolonged red blood cell lifespan	Increased
Vitamin B12/ folate deficiency	Decreased erythropoiesis	Increased
Recent blood loss (including blood donation), Haemolytic anaemia	Increased erythropoiesis	Decreased
Recent blood transfusion	Potential dilution with transfused blood	Decreased
Chronic renal failure	Reduced red blood cell lifespan, use of erythropoietin	Decreased
Chronic liver disease	Increased erythropoiesis	Decreased
Pregnancy[7]	Increased red blood cell turnover	Decreased

4. Both venous blood and capillary blood samples are suitable for HbA1c testing. Mainframe analysers in labs and Point of Care Testing (POCT) devices that are National Glycohaemoglobin Standardization Programme (NGSP) - certified and conform to the Health Sciences Authority's External Quality Assurance Programme (EQAP) should be used for screening diabetes. Licensees of healthcare institutions will also receive an email notification via the E-Licensing for Healthcare (eLIS) system providing more details on the regulatory requirements for onsite HbA1c testing.

5. Doctors who prefer to use the FPG or the OGTT for the screening and diagnosis of diabetes mellitus may continue to do so.

[6] Thalassaemia, with a local population prevalence of 4%, is the most common genetic blood disorder.

[7] HbA1c is not recommended for screening of Gestational Diabetes Mellitus. Doctors may refer to the Appropriate Care Guidelines 'Gestational Diabetes Mellitus – An update on screening, diagnosis and follow-up' issued in May 2018 for more details.

ANNEX D

USE OF NON-FASTING LIPID PROFILE AS AN ALTERNATIVE INITIAL SCREENING TEST FOR LIPID DISORDERS

1. All doctors should note that **the non-fasting lipid profile may be used as an alternative initial screening test for lipid disorders.** This is in line with international guidelines adopted by a number of countries and organizations including the UK National Institute for Health and Care Excellence (NICE), the New Zealand Ministry of Health, the Canadian Cardiovascular Society, the European Atherosclerosis Society, and the European Federation of Clinical Chemistry & Laboratory Medicine.

2. Existing literature show that non-fasting Triglycerides (TG) are on average, between 0.1mmol/L to 0.3mmol/L **higher** than fasting TG. Non-fasting Low-Density-Lipoprotein Cholesterol (LDL-C) are on average between 0.1mmol/L to 0.3mml/L **lower** than fasting LDL-C.

3. Given that the mean differences between fasting and non-fasting samples is minimal, there are no changes to the current diagnostic and management thresholds.

4. Doctors should consider performing fasting lipid profiles instead of non-fasting lipid profiles whenever there is an uncertainty over the potential validity of the results, especially if pharmacological therapy is being considered. For example:

(a) High fat consumption prior to test which leads to abnormally high TG readings. Markedly high TG readings (≥4.5mmol/L) in turn would invalidate calculated LDL-C levels (based on the Friedewald formula).

(b) Borderline TG or LDL-C levels: Some individuals with borderline high TG levels in the non-fasted state may have normal TG levels in the fasted state. Similarly, some individuals with borderline normal LDL-C levels in the non-fasted state may actually have elevated LDL-C levels in the fasted state.

5. Only venous blood samples will be permitted for testing by mainframe analysers as the use of POCT devices for the screening of lipid disorders has yet to be validated.

6. Doctors who prefer to use fasting lipid tests for the screening of lipid disorders may continue to do so.

7. In view of the allowance of the non-fasting lipid profile as an alternative initial screening test for lipid disorders, an addendum to the 2016 MOH Lipids Clinical Practice Guidelines would be published on MOH's website.

ANNEX E

USE OF HUMAN PAPILLOMAVIRUS (HPV) TEST AS THE PRIMARY SCREENING TEST INSTEAD OF PAP SMEAR FOR WOMEN AGED 30 YEARS AND ABOVE

1. All doctors should note that **Human Papillomavirus (HPV) testing is recommended as the primary screening test for women aged 30 years and above at a screening interval of five years**[8]. The method of sample collection remains the same.

2. The current guidelines recommend that women aged 25-69 years, who have ever had sex, undergo Pap smear as the primary screening test, once every 3 years. However, recent studies have shown that the HPV test is more sensitive and cost effective than the Pap smear. The case for HPV testing to replace Pap smear is further supported by studies showing that most cases of carcinoma-in-situ (CIN) and cervical cancer are preceded by HPV infection[9]. A negative HPV test would therefore only require a repeat test in five years.

3. However, because of the high prevalence of HPV infection among women between the ages of 25 to 29 years, HPV testing in this age band would lead to increased colposcopies and unnecessary interventions, especially when approximately 90% of those infected with HPV will clear acquisition spontaneously within 2 years. Therefore, **Pap smears performed at three yearly intervals, remain the recommended primary screening test for women aged 25 to 29 years.**

4. The possible outcomes of a HPV test and the corresponding follow-up actions and potential benefits are summarized in Table 3.

Table 3: Summary of outcomes, follow up actions, and potential benefits of primary HPV testing (among women aged 30 years and above)

Outcomes	Follow-up actions	Benefits
Positive for HPV 16/18[10]	Refer to SOC for further investigation with colposcopy.	If found to have CIN or cervical cancer on colposcopy, would benefit from timely treatment. If colposcopy was negative, would still benefit from closer monitoring.
Positive for non-HPV 16/18	Sample collected through liquid based cytology (LBC) for HPV testing will be used to perform a pap smear for cytological examination (results determine further follow-up action).	If found to have CIN or cervical cancer on colposcopy, would benefit from timely treatment. If colposcopy was negative, would still benefit from closer monitoring.
Negative for HPV	Five yearly HPV screening.	Reduced frequency of screening from 3 yearly to 5 yearly.

[8] Under SFL, subsidies for HPV tests are available for women up to 69 years of age.
[9] HPV infection may precede CIN by >5 years and cervical cancer by between 10-30 years.
[10] HPV types 16 and 18 together cause approximately 70% of call cervical cancer cases.

Figure 1: Summary of follow up actions after initial HPV screening test