MOH Circular No. 36/2025



MH 78:83

19 June 2025

Please refer to distribution list

KEY AMENDMENTS TO THE MORATORIUM ON GENETIC TESTING AND INSURANCE

The Ministry of Health (MOH) and the Life Insurance Association (LIA) introduced the 'Moratorium on Genetic Testing and Insurance' in October 2021 ("2021 Moratorium") to prevent individuals from being deterred to undergo clinical genetic testing for medical indications and/or from participating in precision medicine (PM) research due to concerns on the use of genetic test results in insurance underwriting.¹

2. To support the launch of the national Familial Hypercholesterolaemia (FH) genetic testing programme ("FH Programme") on 30 June 2025, MOH and LIA have amended the Moratorium ("2025 Moratorium") to enhance protections for individuals undergoing genetic testing for FH under the FH Programme. The FH Programme aims to support early identification and interventions for individuals with FH, and forms part of MOH's broader preventive care efforts. For more information on the FH Programme, please refer to the MOH Circular No. 33/2025, 'Introduction of Familial Hypercholesterolaemia (FH) Genetic Testing Service' (Annex A).

3. The 2025 amendments introduce specific provisions related to FH genetic testing conducted under the FH Programme while preserving the core protections of the 2021 Moratorium.

Key Amendment of 2025 Moratorium

4. The key amendment under the 2025 Moratorium is to expressly **prohibit the use and disclosure of results of all FH genetic tests**² (both predictive and diagnostic) taken under the FH Programme.

¹ MOH Circular No. 08/2021 'Moratorium on Genetic Testing and Insurance: Ban on the Use of Genetic Test Results from Biomedical Research in Insurance Underwriting' and MOH Circular No. 100/2021, 'Moratorium on Genetic Testing and Insurance'

² Such as *LDLR*, *APOB*, and *PCSK9* genes only in the FH panel screening tests conducted under the FH Programme

5. All other provisions of the 2021 Moratorium remain unchanged and in effect. A summary of the key provisions of the 2025 Moratorium is provided in <u>Annex B</u>. The full document can be accessed via this link: <u>https://go.gov.sg/moratorium-on-genetic-testing-and-insurance</u>.

6. This also does not impact the current practice of insurers requesting for patients' diagnosis when it has been made by the healthcare professionals or institutions. Hence, in this context, insurers can request the disclosure of and/or use the diagnosis of FH condition, when it has either been made based on clinical assessment or via the FH genetic test.

Supporting Documents

7. To accompany this Moratorium, a professional guidance document has been developed to clarify the scope and protections under the Moratorium for clinicians and genetic counsellors (<u>Annex C</u>). In addition, a consumer guide aimed at raising public awareness and understanding of the Moratorium is available via this link: <u>https://go.gov.sg/moratorium-on-genetic-testing-and-insurance</u>.

Implementation Timeline

8. The 2025 Moratorium will take effect from **30 June 2025**. Licensees, registered medical practitioners and research institutions are to take note of the amendments and make any necessary changes to their current processes where appropriate. This may include providing patients with the consumer guide and advising them that their FH genetic tests taken are not disclosable to their insurers prior to referring them to the FH Programme.

9. Should you require further clarification, please email us at <u>HCSA_Enquiries@moh.gov.sg</u>.

Thank you.

PROF KENNETH MAK DIRECTOR-GENERAL OF HEALTH MINISTRY OF HEALTH

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All General Practitioners Clinics (CHAS and non-CHAS)

Primary Care Networks

All Registered Doctors

All Licensees of Clinical Laboratory Service

All Research Institutions Notified under the Human Biomedical Research Act (HBRA)

Annexes

Annex A	MOH CIRCULAR NO. 33/2025, 'INTRODUCTION OF FAMILIAL HYPERCHOLESTEROLAEMIA (FH) GENETIC TESTING SERVICE'
Annex B	KEY PROTECTIONS OF THE 2025 MORATORIUM
Annex C	PROFESSIONAL GUIDANCE ON THE MORATORIUM



MH 70:26/1

MOH Circular No. 33/2025

09 June 2025

Please refer to distribution list

INTRODUCTION OF FAMILIAL HYPERCHOLESTEROLAEMIA (FH) GENETIC TESTING SERVICE

This circular informs healthcare institutions and registered medical practitioners on the introduction of Familial Hypercholesterolaemia (FH) Genetic Testing as a mainstream clinical service from 30 June 2025.

FAMILIAL HYPERCHOLESTEROLAEMIA

2. FH is an inherited genetic condition that predisposes FH patients to early onset atherosclerotic cardiovascular disease (ASCVD) due to impaired low-density lipoprotein cholesterol (LDL-C) metabolism. FH affects an estimated 20,000 Singapore residents and carries a high risk of major adverse cardiovascular events, leading to significant morbidity and mortality. Early detection through index genetic testing and cascade screening, and intervention through the administration of intensive lipid-lowering therapies can substantially reduce the risk of cardiovascular complications and improve outcomes.

SERVICE OVERVIEW

3. In line with the Ministry of Health (MOH)'s efforts to enhance preventive care, a new FH Genetic Testing service will be introduced to support early identification of patients with FH. This will involve the following:

- a) Establishment of the Genomic Assessment Centre (GAC);
- b) Identification of high-risk index patients and referral to the GAC by physicians (based on the GAC FH referral criteria);
- c) Genetic testing of these referred patients ("FH index genetic testing") at the GAC; and
- d) Subsequent screening for first-degree relatives of patients who test positive for FH ("cascade screening").

4. On initial roll-out, only Singapore Citizens / Permanent Residents (SCs/PRs) will be eligible for genetic testing at the GAC. This applies to both FH index genetic testing and cascade screening.

ESTABLISHMENT OF THE GAC

5. The GAC is the specialised facility for genetic testing services within each cluster. The GAC will serve as a dedicated clinic where patients can undergo genetic testing and receive genetic counselling to understand the benefits and implications of genetic testing and facilitate cascade screening of family members. Physicians may start referring patients who meet the referral criteria for FH index genetic testing to the first GAC operated by Singapore Health Services (SingHealth) from <u>30 June 2025</u>. This GAC will serve all Singapore residents until additional centres open. GACs operated by National Healthcare Group (NHG) and National University Health System (NUHS) will be established within the next year.

GAC REFERRAL CRITERIA FOR FH INDEX GENETIC TESTING

6. For FH index genetic testing at the GAC, SCs/PRs may be referred only if they meet the criteria of <u>LDL-C \geq 5.5 mmol/L (\geq 212 mg/dL)</u> ("GAC FH referral criteria"). Please refer to <u>Annex A-1</u> for a flowchart of the consolidated referral criteria and subsidy criteria for FH index genetic testing in the GAC.

7. In order for the GAC to verify the referred patient's eligibility based on LDL-C cut-off, referring physicians should:

- a) Indicate the referred patient's LDL-C level and date of the LDL-C test in the referral letter to the GAC; and
- b) Ensure that the medical/laboratory report documenting the referred patient's LDL-C level is available on the National Electronic Health Records (NEHR) or attach a copy of the report with the referral letter to the GAC. Physicians may also advise their patients to bring a copy of their medical/laboratory report to their GAC appointment for verification.

8. For more details regarding referral workflows from various referral sources to the GAC, please refer to **Annex B** and the guide for genetic testing and management of FH in primary care, which will be circulated to all primary care physicians (PCPs) separately.

CLINICAL WORKFLOW

9. Upon verification of the referred patient's eligibility for FH index genetic testing, the GAC will conduct the following (refer to <u>Annex C</u> for a diagram of the clinical workflow):

- a) Pre-genetic test counselling, financial counselling, consent-taking;
- b) FH index genetic testing via an FH gene panel comprising of the LDLR, APOB, and PCSK9 genes only;
- c) Post-genetic test counselling and uploading of a GAC report to NEHR, with a copy of the report provided to the patient;¹ and

¹ Genetic test results will be accessible via the patient's NEHR and HealthHub. A separate GAC report will also be accessible via the patient's NEHR under the referral notes section, with a copy provided to the patient.

d) Cascade screening for eligible and consenting SC/PR first-degree relatives (i.e., parents, siblings, and children) if the referred patient tests positive for a pathogenic variant in any one of the three FH-associated genes analysed during FH index genetic testing.

DIAGNOSIS AND MANAGEMENT OF SUSPECTED AND CONFIRMED FH

10. The diagnosis of FH in a patient who tests positive for a pathogenic variant in an FH-associated gene will be made in conjunction with the presence of a suggestive clinical history, physical examination and/or abnormal non-genetic laboratory tests (i.e., raised LDL-C levels). The diagnosis of FH may be aided by the Dutch Lipid Clinic Network Score (DLCNS) for FH.

11. The clinical management of hypercholesterolaemia, regardless of the status or results of the genetic testing, shall remain the responsibility of the referring physician. Physicians are recommended to manage patients with hypercholesterolaemia in accordance with prevailing national guidelines.² This includes, but is not limited to:

- a) Non-pharmacological management of hypercholesterolaemia;
- b) Pharmacological management of hypercholesterolaemia;
- c) Assessment for the clinical diagnosis of FH;
- d) Ruling out of secondary causes of hypercholesterolaemia where relevant;
- e) Clinical and biochemical monitoring of lipid control;
- f) Tracing of genetic test results and adjustment of patient's treatment and LDL-C targets; and
- g) Referral to relevant specialists for special patient populations if required (e.g., paediatric endocrinology for paediatric patients).

12. As much as possible, referring physicians should **encourage eligible patients and first-degree relatives to receive FH index genetic testing and cascade screening respectively**, so that proactive measures can be taken to reduce ASCVD risk.

13. In the event where a patient tests positive for a pathogenic variant in an FHassociated gene but is not on active follow-up (e.g., if the patient was identified through cascade screening), the GAC will advise the patient to visit a PCP for follow-up.

² Agency for Care Effectiveness (ACE). Lipid management: focus on cardiovascular risk. ACE Clinical Guidance (ACG), Ministry of Health, Singapore. Available from: go.gov.sg/acg-lipid-management

SUBSIDIES AND MEDISAVE USE FOR FH GENETIC TESTING

Subsidy at the GAC

14. To qualify for subsidised FH genetic testing, **<u>index patients</u>** must meet the GAC FH referral criteria (para 6) <u>and</u> be referred from one of the following eligible referral sources:

- i. CHAS GP clinics, for CHAS/PG/MG cardholders only; or
- ii. Polyclinics; or
- iii. Subsidised SOC in PHIs

15. First-degree SC/PR relatives of an index patient who tested positive for FH at the GAC can receive subsidies for cascade screening. For avoidance of doubt, first-degree relatives of an unsubsidised index patient are eligible to receive subsidy for the cascade screening. Means-tested subsidies of up to 70% under the SOC subsidy framework will be provided to eligible patients.

16. SCs / PRs who meet the GAC FH referral criteria but not the subsidy criteria may still undergo unsubsidised FH genetic testing at the GAC.

MediSave use at the GAC

17. Both subsidised and unsubsidised patients who meet the GAC FH referral criteria can tap on MediSave under the MediSave500/700 scheme, as part of the Chronic Disease Management Programme (CDMP). The amount of MediSave utilised is subject to the prevailing 15% copayment for CDMP. Patients and first-degree relatives who are 60 years old and above may also utilise Flexi-MediSave to offset any remaining cost. Typically, only patients diagnosed with one or more CDMP conditions may tap on the MediSave 500/700 limits for treatments under the CDMP. Nevertheless, MOH will allow an exception for first-degree relatives, who are identified for FH cascade screenings, to also tap on the MediSave 500/700 limits even if they are not diagnosed with a CDMP condition. This arrangement seeks to facilitate quicker access to MediSave for patients requiring such screenings, and will stand until further notice.

Summary of Subsidy and MediSave eligibility at GAC

18. For reference, **Annex A-1** provides a diagrammatic overview of the citizenship criteria, GAC FH referral criteria, and subsidy criteria for index patients. **Annex A-2** provides a diagrammatic overview of the cascade testing criteria at the GAC.

Subsidy and MediSave eligibility for follow-up care

19. <u>Follow-up at primary care.</u> Patients who test positive for FH and seek follow-up at primary care may be eligible for subsidies and to tap on MediSave (under the MediSave 500/700 limits), depending on the criteria in the specific setting where care is sought, per <u>Table 1</u>.

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Care setting	Subsidy eligibility	MediSave eligibility
Polyclinics	SCs and PRs receive up to 75% subsidy for drugs and services	SCs and PRs can claim under MediSave500/700 subject to 15% co-payment requirement.
Healthier SG (HSG) GP to whom patient is enrolled	 Enrolees who are PG/MG/CHAS cardholders receive: Percentage-based HSG Chronic Tier subsidies* for drugs on the HSG Medication List Dollar-based subsidies for other care components *Percentage-based subsidies for some drugs on the HSG Medication List are available only for CHAS Blue/Orange cardholders, or PG/MG cardholders who also hold a CHAS Blue/Orange card. 	Flexi-MediSave may also be used to cover any remaining copayment, including the 15% co-payment for claims for CDMP treatment. 15% cash co-payment waived for HSG enrolees at their enrolled clinic
Other CHAS GPs	PG/MG/CHAS cardholders receive dollar-based CHAS subsidies	SCs and PRs can claim under MediSave500/700 subject to 15% co-payment requirement. Flexi-MediSave may also be used to cover any remaining copayment, including the 15% co-payment for claims for CDMP treatment.

Table 1. Subsidy and MediSave eligibility at different primary care settings

20. Follow-up at SOCs.

- a) **Index patients** who are referred to an SOC for follow-up will be subsidised for their follow-up treatment, if the referral meets the subsidised referral criteria.
- b) For **cascade patients**, whose care episode did not originate from a PCP, they will be advised to follow-up with a PCP. If they are subsequently referred by the PCP to follow up at an SOC, they can be subsidised for the follow-up treatment if the referral meets the subsidised referral criteria.

MEDISAVE CLAIM SUBMISSION

21. National Platform for Healthcare Claims (NPHC) has been enhanced from 1 June 2025 to allow for MediSave claims³ for FH index genetic testing and cascade screening. For such claims, please use the following charge code – diagnosis code pairings in **Annex D**. MediSave claims should only be done at GACs after they have commenced operations.

PRICES FOR FH TESTING

22. The indicative price range for the (i) visit at the GAC and (ii) potential follow-up treatment are summarised in **Annex E**. Primary care providers and the GAC should convey the indicative price range to patients during consultations or financial counselling where relevant.

FOR CLARIFICATIONS

23. For any clarifications on this circular, please email <u>moh_info@moh.gov.sg</u>.

PROFESSOR KENNETH MAK DIRECTOR-GENERAL OF HEALTH MINISTRY OF HEALTH

³ MOH Healthcare Claims Portal (MHCP) will also be enhanced to allow GPs to submit MSV claims for cascade screening cases through additional selection of diagnosis code.

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All General Practitioners Clinics (CHAS and non-CHAS)

Primary Care Networks

All Registered Doctors

<u>Annexes</u>

Annex A-1	Consolidated Referral & Subsidy Criteria for FH Index Genetic Testing in the GAC
Annex A-2	Consolidated Clinical & Subsidy Criteria for Cascade Screening in
	the GAC
Annex B	Referral Source & Workflow
Annex C	Clinical Workflow for FH Index Genetic Testing in the GAC
Annex D	Charge Code and Diagnosis Pairings (for MSV)
Annex E	Indicative Price Ranges for FH Testing and Follow-Up Care
Annex F	Frequently Asked Questions (FAQs)

Consolidated Referral & Subsidy Criteria for FH Index Genetic Testing in the GAC



<u>Abbreviations</u>: CHAS, Community Health Assist Scheme; GAC, Genomic Assessment Centre; GP, General Practitioner; HSG, Healthier-SG; LDL-C, low-density lipoprotein cholesterol; MG, Merdeka Generation; PG, Pioneer Generation; PHI, Public Healthcare Institutions; SOC, Specialist Outpatient Care (Clinic); SC/PR, Singapore Citizen / Permanent Resident.

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⁴ Historical or overseas LDL-C test results indicating levels \geq 5.5 mmol/L are allowed but must be well-documented, and these reports should be included in the referrals to the GAC.

Consolidated Clinical & Subsidy Criteria for Cascade Screening in the GAC



Abbreviations: GAC, Genomic Assessment Centre; SOC, Specialist Outpatient Care (Clinic); SC/PR, Singapore Citizen / Permanent Resident

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⁵ The subsidy status of the cascade patient is independent of the index patient (i.e., first-degree relative). For an index patient who undergoes index genetic testing at a private (non-subsidised rate), the private index patient's first-degree relatives can still receive subsidised cascade screening at the GAC.

Annex B

Referral Source & Workflow

Referral Source	Subsidised at GAC (for index patients)?	Referral Workflow	
Primary Care			
CHAS GPs		HSC CDa Via Clinia Management System (proferred) or	
- CHAS, PG, MG cardholders	Yes	Non HSC CDo Vio CHAS Poterral Form	
- Non-CHAS/PG/MG cardholders	No	NOII-1130 GFS VIA CHAS REIEITAI FOITI	
Non-CHAS GPs	No	E-mail to KKH central appointment at centralappt@kkh.com.sg	
SingHealth Polyclinics	Yes	E-mail to KKH central appointment at referral@kkh.com.sg	
Non-SingHealth Polyclinics	Yes	E-mail to KKH central appointment at centralappt@kkh.com.sg	
SOCs			
SingHealth SOCs			
- Subsidised clinic Yes		E-mail to KKH central appointment at referral@kkh.com.sg	
- Private clinic	No		
Non-SingHealth PHIs' SOCs			
- Subsidised clinic Yes		E-mail to KKH central appointment at referral@kkh.com.sg	
- Private clinic	No		
Private Hospitals/Clinics	No	E-mail to KKH central appointment at centralappt@kkh.com.sg	

Abbreviations: CHAS, Community Health Assist Scheme; GP, General Practitioner; MG, Merdeka Generation; PG, Pioneer Generation; PHI, Public Healthcare Institutions; SOC, Specialist Outpatient Care (Clinic).

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Clinical Workflow for FH Genetic Testing in the GAC



Abbreviations: LDL-C, low-density lipoprotein cholesterol; SC/PR, Singaporean Citizen or Permanent Resident; NEHR, National Electronic Health Records

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Annex C

Annex D

Charge code – Diagnosis pairings for FH testing and screening

	Charge code	Diagnosis code		
<u>FH index</u> <u>genetic testing</u>	CV0003 if patient has Lipid Disorder (hyperlipidaemia) only Or CC0003 if patient has Lipid Disorder (hyperlipidaemia) (e.g. Familial Hypercholesterolaemia) complicated by Peripheral Vascular Disease (I739)	 E780 – E785, I739 (based on patient's medical history) E780 Pure hypercholesterolaemia E781 Pure hyperglyceridaemia E782 Mixed hyperlipidaemia E783 Hyperchylomicronaemia E784 Other hyperlipidaemia E785 Hyperlipidaemia, unspecified Peripheral vascular disease, I739 unspecified 		
FH cascade screening for first degree relatives	CV0003	Z01Other special examinations and investigations of persons without complaint or reported diagnosis		

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Indicative price ranges for FH testing and fol	low-up care	
Pre-subsidy price	After subsidies	After subsidies

				Alter Subsidies	and MSV500^
GAC visit*	Proband		\$764	\$117 - \$575	\$18 - \$87
	Ca	ascade	\$334	\$53 - \$253	\$8 - \$38
	Pre-s	ubsidy price (annual basi	s)	After subsidies	After subsidies and MSV500^
Follow-up treatment at	Polyclinics^^	Only statins and/or Ezetimibe	\$146 - \$292	\$19 - \$220	\$0
primary care		Statins, Ezetimibe and Evolocumab	\$3298	\$414 - \$3226	\$0 - \$2726
	HSG GP where	Only statins and/or Ezetimibe	\$146 - \$292	\$19 - \$146	\$0
	enrolled^^	Statins, Ezetimibe and Evolocumab	\$3298	\$414 - \$3152	\$0 - \$2652
	For Non-HSG CHAS GP or HSG GP where patient is not en			rolled pre-subsidy	prices are as

es are as CHAS GP or HSG GP where patient is not enrolled, pre-subsidy pi determined by clinics. CHAS dollar-based subsidies will apply to CHAS cardholders

*Comprises pre-screening counselling, phlebotomy, FH screening test, and post-screening counselling

^Assumes patient does not have a complex chronic CDMP condition, and has full MSV500 balance left; otherwise, the annual limit will be \$700 instead. Seniors of 60 years old and above may also utilise Flexi-MediSave to pay for the remaining cost in addition to MSV500/700.

MAssumes patient is enrolled under HSG at polyclinic or HSG GP for wavier of 15% co-payment for CDMP

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Frequently Asked Questions (FAQs)

I. <u>Referral criteria for FH genetic testing at GACs</u>

1. Why is the LDL-C cut-off for GAC FH referrals set at ≥ 5.5 mmol/L (≥ 212 mg/dL)?

- This LDL-C cut-off in the GAC FH referral criteria takes into account epidemiological data from existing national screening programmes and the Precision Health Research Singapore (PRECISE) Clinical Implementation Pilot (CIP) on FH, vis-à-vis the projected capacity of the designated GAC at initial roll-out.
- Medical practitioners should note that <u>the LDL-C cut-off in the GAC FH referral</u> <u>criteria differs from the LDL-C cut-off to clinically suspect FH</u>. As stated in current Agency for Care Effectiveness (ACE) Clinical Guidance for Lipid Management,⁶ FH should be suspected when LDL-C levels are > 4.9 mmol/L (> 190 mg/dL) in adults after excluding secondary causes.
- Following implementation, MOH will continue to review the GAC FH referral criteria and genetic testing protocols and will update clinical workflows as appropriate.
- For patients with LDL-C > 4.9 mmol/L (> 190 mg/dL) to < 5.5 mmol/L (< 212 mg/dL) who may benefit from genetic testing but do not meet the GAC referral criteria, refer to question 2 below.

Can patients with LDL-C > 4.9 mmol/L to < 5.5 mmol/L (> 190 mg/dL to < 212 mg/dL) be referred to GAC for subsidised FH genetic testing if there is clinical suspicion for FH?

- Genetic tests for FH done <u>outside</u> of the GAC will not be eligible for the subsidies stated in this circular.
- Physicians should not refer patients who do not meet the referral criteria of LDL-C ≥ 5.5 mmol/L (≥ 212 mg/dL) to the GAC.
- Physicians may consider referring patients who do not meet the referral criteria but may benefit from FH genetic testing to a relevant specialist <u>outside</u> of the GAC (as per the usual process for SOC referrals) for further evaluation.

3. Can patients with historical LDL-C results of \geq 5.5 mmol/L (\geq 212 mg/dL) be referred to the GAC?

- Patients with historical LDL-C results of ≥ 5.5 mmol/L (≥ 212 mg/dL) (e.g., dated several years ago) can be referred to the GAC if these historical LDL-C results are clearly documented on an unambiguous and objective medical/laboratory report.
- In principle, these patients should be investigated for FH even if their current LDL-C results are < 5.5 mmol/L (< 212mg/dL) (regardless of whether they are currently on lipid-lowering therapy or not).

⁶ Agency for Care Effectiveness (ACE). Lipid management: focus on cardiovascular risk. ACE Clinical Guidance (ACG), Ministry of Health, Singapore. Available from: go.gov.sg/acg-lipid-management

4. Can patients with overseas LDL-C results of \geq 5.5 mmol/L (\geq 212 mg/dL) be referred to the GAC?

- The GAC can accept LDL-C tests done overseas if the referral criteria of ≥ 5.5 mmol/L (≥ 212 mg/dL) is met.
- The overseas LDL-C results should be clearly documented on an unambiguous and objective medical/laboratory report.

5. Can first-degree relatives (of patients who test positive for a pathogenic variant for FH) be referred directly to the GAC for cascade screening?

- For patients who receive FH index genetic testing in the GAC, if a pathogenic variant in any one of the three FH-associated genes (i.e., any of LDLR, APOB or PCSK9), the GAC will contact first-degree relatives of the patient (subject to the patient's consent) for cascade screening.
- In the event that a patient receives FH index genetic testing <u>outside</u> of the GAC and tests positive for a pathogenic variant for FH, first-degree relatives cannot be referred directly to the GAC for cascade screening. To note, first-degree relatives who have LDL-C levels that meet the referral criteria of LDL-C ≥ 5.5 mmol/L (≥ 212 mg/dL) can be referred to the GAC for FH index genetic testing.
- Following implementation, MOH will continue to review referral criteria and workflows to the GAC and will update clinical workflows as appropriate.

II. <u>Referral source, subsidy criteria and MediSave use</u>

6. Will all patients who are referred to GAC receive subsidies for FH genetic testing?

- No. Patients must meet all of the subsidy criteria stated in this circular to be eligible for subsidies.
- Patients who meet the GAC FH referral criteria (≥ 5.5 mmol/L (≥ 212 mg/dL)), but do <u>not</u> meet all of the subsidy criteria, may still be referred to GAC for <u>non-subsidised</u> FH genetic testing (e.g., referrals from non-CHAS GP / private SOC in PHI / private hospitals).
- Patients and first-degree relatives who meet the referral criteria, will be eligible to claim MediSave regardless of their subsidy status.

7. Will named referrals to the GAC be allowed?

- The GAC will primarily be staffed by Genetic Counsellors (GC), Genetic Counselling Associates (GCA), and executives. As such, named referrals are not applicable to GAC referrals since patients will not be under the care of any specific specialist.

III. Genetic testing

8. For index genetic testing, will other FH-associated genes (other than *LDLR*, *APOB*, *PCSK9*) be reported?

- No, only the above stated genes will be analysed and reported in both the lab report and the GAC report.
- There are well-studied FH-causing pathogenic mutations for *LDLR*, *APOB*, *PCSK9* genes. In addition, these three genes have high penetrance and an autosomal dominant inheritance pattern with clear benefits for cascade screening.

9. For cascade screening, what genes will the patient's first-degree relatives be tested for?

- Only the specific gene with an identified pathogenic variant in the index patient will be tested as part of cascade screening of their first-degree relatives.

IV. Clinical management of FH

10. How does the clinical management of FH differ from that of non-familial hypercholesterolaemia?

- A patient's LDL-C target should be determined based on cardiovascular risk.
- In patients with FH, intensive lipid-lowering therapy should be considered, using maximally-tolerated statin and adding ezetimibe as needed. Further addition of PCSK9 monoclonal antibody or inclisiran for further risk reduction should be based on LDL-C level and clinical need. For further details, please refer to ACE Clinical Guidance "Lipid management: focus on cardiovascular risk"⁷ or the guide on FH Genetic Testing and management in Primary Care.
- Evolocumab, a PCSK9 inhibitor, has been included under the MOH Medication Assistance Fund (MAF) since September 2023⁸ and will be included in the <u>Healthier SG Medication List</u> (for enhanced subsidies under Healthier SG Chronic Tier) from 2 June 2025. The MAF clinical criteria of evolocumab 140mg/mL solution for injection in prefilled autoinjector are:
 - non-FH or mixed dyslipidaemia, with ASCVD and additional risk factors and LDL-C level above 1.8 mmol/L despite maximal tolerated lipid-lowering therapy (LLT) for at least 12 weeks; or
 - heterozygous FH (HeFH), with ASCVD and LDL-C level above 1.8 mmol/L despite maximal tolerated LLT for at least 12 weeks; or
 - HeFH, without ASCVD, and LDL-C level above 2.6 mmol/L despite maximal tolerated LLT for at least 12 weeks; or
 - homozygous FH (HoFH) with LDL-C level above 1.8 mmol/L despite maximal tolerated statin-lowering therapy for at least 12 weeks.

11. How should patients who are assessed to have clinical FH based on the DLCNS but have a negative FH genetic test result but be managed?

 ⁷ Agency for Care Effectiveness (ACE). Lipid management: focus on cardiovascular risk. ACE Clinical Guidance (ACG), Ministry of Health, Singapore. Available from: go.gov.sg/acg-lipid-management
 ⁸ For more information, physicians may refer to the Technology Guidance from the MOH Drug Advisory Committee published by Agency for Care Effectiveness: https://www.ace-hta.gov.sg/docs/default-source/drug-guidances/pcsk9-inhibitors-for-treating-hypercholesterolaemia.pdf?sfvrsn=a54248fc_4.

- Patients who undergo genetic testing at the GAC will receive a GAC report which includes treatment recommendations. This includes patients whose genetic test results are negative for known pathogenic variants for FH.
- Physicians are advised to refer to the treatment recommendations within the GAC report when considering further management of their patients.
- A diagnosis of clinical FH based on clinical diagnostic tools for FH such as the DLCNS in the absence of a positive FH genetic test result may be attributed to less common FH-associated genetic mutations, currently unknown genetic associations, or other rare causes (e.g., sitosterolaemia).
- If patients meet the criteria for clinical FH, it is recommended that they are treated as for FH in view of likely elevated risk of atherosclerotic cardiovascular disease.
- Physicians should refer to prevailing national guidelines on the management of patients with hypercholesterolaemia in general.
- Physicians may consider a referral to a specialist for further assessment where necessary.

12. How should management and cascade screening be approached for a patient with a result of "variant of uncertain significance" on the GAC report?

- Recommendations on cascade screening and treatment are included in the GAC report for patients found to have a variant of uncertain significance (VUS).
- Physicians are advised to refer to the treatment recommendations within the GAC report when considering further management of their patients.
- VUS refers to a genetic change or mutation that has been identified, but its clinical significance is currently unclear. Reclassification of the variant may occur over time as more data becomes available.
- A VUS result does not confirm a diagnosis of familial hypercholesterolemia and testing family members for a VUS to guide their medical management is not recommended.
- Patients with a VUS may still be assessed to have clinical FH based on clinical diagnostic tools for FH such as the DLCNS and should be managed accordingly based on their clinical symptoms, family history, and other risk factors.
- Physicians should refer to prevailing guidelines like the ACE Clinical Guidance for lipid management on the management of patients with hypercholesterolaemia in general.
- Physicians may consider a referral to a specialist for further assessment where necessary.

13.Under what circumstances should I refer patients to a specialist for management of hypercholesterolaemia?

- In line with MOH's overall direction, management of hypercholesterolaemia should be anchored in primary care as much as possible (regardless of a FH diagnosis).
- Complex patients may be referred to specialists for further management, at the primary provider's discretion (e.g., if patients are unable to tolerate conventional therapy, or are unable to achieve target LDL-C despite being on maximal

therapy). Please refer to the guide for on FH Genetic Testing and management in Primary Care for more details.

14. How should hypercholesterolaemia (including FH) be managed in paediatric patients (< 18 years old)?

- The clinical and biochemical criteria (i.e., LDL-C cut-off) to suspect FH in paediatric patients differs from that of adults. Most guidelines adopt different LDL-C cut-offs depending on whether there is family history of high cholesterol, premature ASCVD or known pathogenic variant for FH.
- A referral to a relevant specialist (e.g., paediatric endocrinologist) should be considered, especially if lipid-lowering therapy is warranted.

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KEY PROTECTIONS OF THE 2025 MORATORIUM

Table 1: Summary of Types of Genetic Test / Information and Use by Insurers

Type of GeneticTest/Information	Individual: Can insurers use the test result?	Family members: Can insurers use the test result?
Direct To Consumer genetic test Genetic test done as part of biomedical research FH genetic tests conducted under the national FH genetic testing programme	No	No
Predictive genetic test	No, unless both conditions in the Moratorium are met: i. The sum assured/pay- out you are applying for is higher than the Approved Financial Limit set out in the Moratorium; and ii. The predictive genetic test you took is one of the Approved Predictive Genetic Test set out in the Moratorium (i.e., HTT genetic test for Huntington's disease and BRCA1/2 genetic test for breast cancer). (See Table 2 for more details)	No

Type of Genetic Test / Information	Individual: Can insurers use the test result?	Family members: Can insurers use the test result?
Diagnostic genetic test Pre-implantation	Yes, however insurers are prohibited from requiring or pressuring an individual	Yes, however insurers are prohibited from requiring or pressuring an individual
genetic diagnosis (PGD), prenatal or newborn genetic screening for congenital diseases	(directly or indirectly) to undertake a diagnostic genetic test as a pre-condition for insurance underwriting.	(directly or indirectly) to undertake a diagnostic genetic test as a pre-condition for insurance underwriting.
Family history	Yes	Yes

Table 2: Conditions which must be met before insurers can request for predictive genetic test results

Approved Insurance Type	CONDITION 1 Above the Approved Financial Limit of (SGD) (aggregated per life basis)	CONDITION 2 Approved Predictive Genetic Test	
Life	\$2,000,000 Sum Assured		
Total Permanent Disability (TPD)	\$2,000,000 Sum Assured	Huntington's Disease	
Long-Term Care (LTC) (≥2 ADLs¹)	\$3,000 Per Month	(HII)	
LTC (1 ADL)	\$3,000 Per Month	Huntington's Disease	
Critical Illness (CI)	\$500,000 Sum Assured	(HTT) Breast Cancer (BRCA1)	
Disability Income (DI)	\$10,000 Per Month	Breast Cancer (BRCA2)	

¹ "Activities of Daily Living" or "ADL" means a set of activities such as (i) bathing or washing, (ii) dressing, (iii) feeding, (iv) transferring, (v) mobility and (vi) toileting.

PROFESSIONAL GUIDANCE ON THE MORATORIUM ON GENETIC TESTING AND INSURANCE

MINISTRY OF HEALTH

JUN 2025

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1. Genetic Testing

- 1.1 Genetic testing refers to the analysis of an individual's human chromosomes, DNA, RNA, to detect gene variants that may be associated with a particular genetic condition, disease susceptibility, or other heritable traits. It can be used to confirm or rule out a suspected genetic condition, help determine a person's chance of developing or passing on a genetic condition, or guide healthcare professionals in choosing the most appropriate treatment.
- 1.2 Genetic testing can be categorised into clinical and non-clinical genetic testing. Clinical and non-clinical genetic testing can be distinguished by: (a) purpose of the genetic test and (b) conditions and terms reported in the test report.
- 1.3 A genetic test would be considered as a clinical genetic test
 - (a) if it is used for any one of the following purposes:
 - to confirm or exclude the presence of a genetic condition in a symptomatic¹ person;
 - (ii) to predict the risk of having affected children;
 - (iii) to predict a genetic condition in an asymptomatic² person for a disease that may occur later in life;
 - (iv) to predict a person's drug response;
 - (v) any purposes that purport to assess, diagnose, prevent, alleviate or treat a medical condition or disorder; or
 - (b) if the test reports conditions and terms which connote meanings similar to medical conditions or induce consumers to seek further medical solutions.
- 1.4 Any genetic testing that performs the same function as clinical genetic testing would be considered clinical, even when there are disclaimers that the genetic test is not used for clinical purposes. For example, some Direct-to-Consumer (DTC) genetic tests may be clinical in nature (e.g., provides risk of certain diseases) despite having disclaimers such as 'the test does not diagnose or predict any health conditions or recommend medical action'.
- 1.5 Clinical genetic tests can be either predictive or diagnostic. A predictive genetic test is a genetic test that predicts a future risk of disease in individuals without symptoms or signs of a genetic disorder (i.e., testing in asymptomatic individuals). On the other hand, a diagnostic genetic test confirms or rules out a diagnosis based on existing symptoms, signs or abnormal non-genetic test results which indicate that the condition in question may be present (i.e., testing in symptomatic individuals). In the same way as a blood test or medical imaging, genetic testing can be used to confirm or exclude diagnoses of ill health.

Example of a Predictive Genetic Test: An asymptomatic individual (i.e., no manifestation of symptoms or signs) who undergoes a genetic test for BRCA1/2 and received a positive test result³.

Example of a Diagnostic Genetic Test: A symptomatic individual (e.g., with lump/mass in breast, or experiencing breast pain) who undergoes a genetic test for BRCA1/2 and received a positive test result.

¹ A symptomatic individual is a person who has observable or detectable signs and symptoms associated with a disease or condition.

² An asymptomatic individual is a person who does not have observable or detectable signs and symptoms associated with a disease or condition.

³ A positive test result means that the genetic test has identified a gene change or genetic mutation in one or more of the genes analysed.

- 1.6 Non-clinical genetic testing refers to genetic testing for non-clinical purposes such as general wellness and recreational purposes, which are not used to assess, diagnose, prevent, alleviate or treat a medical condition or disorder. Some examples of non-clinical genetic testing include:
 - (a) Ancestry testing to provide information about an individual's relatedness to a certain ancestor or ancestral group and/or how much of an individual's genome is likely to have been inherited from ancestors from particular geographical areas or ethnic groups;
 - (b) Innate behavioural/lifestyle testing to provide information about an individual's behavioural propensities or talents, performance capacity (physical or cognitive), or response to certain environmental conditions (e.g. stress); or
 - (c) Nutrigenomics testing to provide information about an individual's response to certain diets.

2. Moratorium on Genetic Testing and Insurance and its Key Protections

- 2.1 In 2021, MOH and Life Insurance Association (LIA) developed the MOH-LIA 'Moratorium on Genetic Testing and Insurance' as part of our efforts to support Precision Medicine (PM) efforts in Singapore. The Moratorium was initially signed in 2021 ("2021 Moratorium") and was later amended and re-signed in 2025 ("2025 Moratorium").
- 2.2 The Moratorium aims to give individuals assurance to undergo clinical genetic testing for medical indications and/or from participating in PM research by protecting the use of certain genetic test results in insurance underwriting. It applies to all relevant LIA members, including life insurers and reinsurers that are licensed to operate in Singapore. The Moratorium on Genetic Testing and Insurance can be accessed <u>here</u>.

2.3 Ban on Genetic Testing as a Pre-Condition for Insurance Underwriting

Under the Moratorium, insurers are prohibited from requiring or pressuring an individual (directly or indirectly) to undertake any genetic test as a pre-condition for insurance underwriting. This applies to ALL genetic tests, including diagnostic, predictive, or prenatal and newborn screening genetic tests.

2.4 Ban on use of Genetic Test Results for Insurance Underwriting

Where an individual has previously undertaken a genetic test, the Moratorium prohibits insurers from requesting for and/or using the following types of genetic test results in insurance underwriting (including health insurance, integrated shield plan, general insurance, group insurance and others):

- i. **[New under 2025 Moratorium]** Familial Hypercholesterolaemia (FH) genetic test results (both predictive and diagnostic) conducted under the national FH genetic testing programme⁴;
- ii. Genetic test results from biomedical research⁵ (regardless of whether the test is predictive or diagnostic);
- iii. Predictive genetic test results, subject to para 2.5 below; and
- iv. Direct-to-Consumer (DTC) genetic tests.

⁴ If an individual takes FH genetic testing outside of the National FH Genetic Testing Programme, insurers cannot request for predictive genetic test results but may request diagnostic genetic test results.

⁵ Regardless of where or when the research was conducted of the nature of the research.

2.5 Conditions where Insurers can Use Predictive Genetic Test Results

Insurers are allowed to request for the disclosure of and/or use predictive genetic test results to underwrite Approved Insurance Types if both the following conditions are met:

- i. The sum assured/pay-out exceeds the Approved Financial Limit set out in the Moratorium; and
- ii. The predictive genetic test is an Approved Predictive Genetic Test set out in the Moratorium (i.e., HTT genetic test for Huntington's disease and BRCA1/2 genetic test for breast cancer).

<u>Table 1: Conditions which must be met before insurers can request for predictive genetic</u> <u>test results</u>

Approved Insurance Type	CONDITION 1 Above the Approved Financial Limit of (SGD) (aggregated per life basis)	CONDITION 2 Approved Predictive Genetic Test	
Life	\$2,000,000 Sum Assured		
Total Permanent Disability (TPD)	\$2,000,000 Sum Assured	Huntington's Disease (HTT)	
Long-Term Care (LTC) (≥2 ADLs ⁶)	\$3,000 Per Month		
LTC (1 ADL)	\$3,000 Per Month	Huntington's Disease (HTT)	
Critical Illness (CI)	\$500,000 Sum Assured	Broast Cancer (BRCA1)	
Disability Income (DI)	\$10,000 Per Month	Dieast Cancel (DRCAZ)	

- 2.6 Insurers are allowed to request for the disclosure of and/or use the following for insurance underwriting:
 - i. Diagnostic genetic test results;
 - Diagnosis of medical condition (regardless of whether the diagnosis was made based on clinical assessment or a genetic test);
 [Example of FH: Insurers are allowed to request the disclosure of and/or use the diagnosis of FH condition (regardless of whether the diagnosis of FH was made based on clinical assessment or a genetic test).]
 - iii. Family history (including whether the applicant has family member(s) with a diagnosed condition); or
 - iv. Predictive genetic test results if the result is favourable to the applicant (whether provided by the applicant or another person, voluntarily or accidentally, or otherwise). Note: The underwriting outcome is at the discretion of the insurers.

3. Counselling Patients on the Use of Genetic Test Results by Insurers

3.1 A consumer guide on the Moratorium can be accessed <u>here</u>. Please refer to Table 2 for a summary of the different types of genetic test / information and whether the use of such information by insurers is prohibited.

⁶ "Activities of Daily Living" or "ADL" means a set of activities such as (i) bathing or washing, (ii) dressing, (iii) feeding, (iv) transferring, (v) mobility and (vi) toileting.

Table 2 [.] Summary	of Types of Genetic Test / Informati	on and Use by Insurers

Type of Genetic Test / Information	Individual: Can insurers use the test result / information?	Family members: Can insurers use the test result / information?		
Direct To Consumer genetic test		No		
Genetic test done as part of biomedical research	No			
FH genetic tests conducted under the national FH genetic testing programme				
Predictive genetic test	No, unless both conditions under para 2.5 are met	No		
Diagnostic genetic test				
Pre-implantation genetic diagnosis (PGD), prenatal or newborn genetic screening for congenital diseases	Yes, subject to para 2.3	Yes, subject to para 2.3		
Family history	Yes	Yes		

4. Handling Patient Enquiries and Complaints

- 4.1 <u>For all disputes/concerns</u>: Patients/consumers may work directly with the insurer to resolve complaint or feedback regarding disputes or suspected non-compliance with the Moratorium.
- 4.2 <u>For complaints on insurance claims</u>: If the patient/consumer and the insurer fail to reach a resolution, he/she may file a complaint at the Financial Industry Disputes Resolution Centre (FIDReC). Alternatively, he/she can approach the Singapore Mediation Centre (SMC) for mediation.
- 4.3 FIDReC serves as the first port of call for consumers who require mediation of claimsrelated disputes arising from the Moratorium (where a customer relationship already exists); consumers will be directed to SMC if there is no existing relationship with the insurer concerned and in the event that FIDReC is unable to handle the cases arising from the Moratorium.
- 4.4 For further queries on the Moratorium, please write in to <u>HCSA Enquiries@moh.gov.sg</u>.

5. Others: Governance of Clinical Genetic Testing Services

5.1 Provision of Clinical Genetic/Genomic Testing Services (CGTS) and Clinical Laboratory Genetic/Genomic Testing Services (LGTS) will be regulated under the Healthcare Services Act (HCSA) to ensure safe and good quality care for patients. A set of guidelines will be published separately.

Case Studies: Examples of Genetic Conditions

	Predictive BRCA1/2 Genetic Test	Diagnostic BRCA1/2 Genetic Test
	[Asymptomatic: e.g., no manifestation of symptoms or signs]	[Symptomatic: e.g., lump/mass in breast, breast pain]
Individual	For life, TPD, LTC, CI, DI insurances:	• Use of genetic test result is left to discretion of individual
Undergoing Genetic Testing	 Positive test result can only be used for underwriting if the double key model is met (i.e., financial limit and list of approved predictive genetic tests) Negative test result may be used for a better underwriting outcome (e.g., to rule out risk from family history) 	insurers
	For all other insurances:	
	Positive test result cannot be used for underwriting	
	 Negative test result may be used for a better underwriting outcome (e.g., to rule out risk from family history) 	
Family	• Genetic test result cannot be used for underwriting all	• Use of genetic test result is left to discretion of individual
Members	insurance policies for family members	insurers, similar to other diagnostic test results

Breast cancer

*If the individual has been diagnosed with breast cancer (whether from clinical assessment or genetic testing), insurers may request for the diagnosis.

Huntington's disease

	Predictive HTT Genetic Test [Asymptomatic: e.g., no manifestation of symptoms or signs]	Diagnostic HTT Genetic Test [Symptomatic: e.g., movement, cognitive or psychiatric symptoms]
Individual Undergoing Genetic Testing	 For life, TPD, LTC, CI, DI insurances: Positive test result can only be used for underwriting if the double key model is met (i.e., financial limit and list of approved predictive genetic tests) Negative test result may be used for a better underwriting outcome (e.g., to rule out risk from family history) 	Use of genetic test result is left to discretion of individual insurers

	For all other insurances:			
	Positive test result cannot be used for underwriting			
	•	Negative test result may be used for a better underwriting		
		outcome (e.g., to rule out risk from family history)		
Family	•	Genetic test result cannot be used for underwriting all	•	Use of genetic test result is left to discretion of individual
Members		insurance policies for family members		insurers, similar to other diagnostic test results

*If the individual has been diagnosed with Huntington's (whether from clinical assessment or genetic testing), insurers may request for the diagnosis.

Familial hypercholesterolaemia (FH)

	FI Pi	H Genetic Test Conducted Outside rogramme	of	the National FH Genetic Testing	FH Na	H Genetic Test Conducted Under ational FH Genetic Testing
Predictive FH Genetic Test [Asymptomatic: e.g., no manifestation of		Diagnostic FH Genetic Test [Symptomatic: e.g., chest pain,		Pr	ogramme	
Individual Undergoing Genetic Testing	•	Positive test result cannot be used for underwriting all insurance policies Negative test result may be used for a better underwriting outcome (e.g., to rule out risk from family history)	•	Use of genetic test result is left to discretion of individual insurers	•	Genetic test result cannot be used for underwriting all insurance policies (both predictive and diagnostic)
Family Members	•	Genetic test result cannot be used for underwriting all insurance policies for family members	•	Use of genetic test result is left to discretion of individual insurers, similar to other diagnostic test results	•	Genetic test result cannot be used for underwriting all insurance policies for family members (both predictive and diagnostic)

*If the individual has been diagnosed with FH (whether from clinical assessment or genetic testing), insurers may request for the diagnosis. ** If a symptomatic individual undergoes FH genetic testing outside of the National FH Genetic Testing Programme, insurers may request for the diagnostic FH genetic test results.