National Genomic Test Directory

Testing Criteria for Rare and Inherited Disease

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国家基因组检测目录

罕见与遗传病检测标准

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Summary

The National Genomic Test Directory identifies the most appropriate test for each clinical indication and the testing methodology by which it should be delivered. The National Genomic Test Directory is set out in a separate excel document available at the following location: https://www.england.nhs.uk/publication/national-genomic-test-directories/

This eligibility criteria document supplements the National Genomic Test Directory by setting out which patients should be considered for testing under that indication and the requesting specialties lists the clinical specialties who would be expected to request the test. The test eligibility criteria provide guidance on which patients may benefit from genomic testing. Tests should only be requested where there is clear evidence that a result is highly likely to change clinical management of the patient or their family. Management includes determining clinical investigations; and/or therapeutic/treatment decisions or strategies; and/or enrolling in nationally approved surveillance programme; and/or informing and supporting reproductive choices.

To develop the National Genomic Test Directory and testing criteria, NHS England convened an expert panel for rare disease. The panel brought together clinicians, scientists, health economists, policy experts, public representatives and patient organisations. The panel developed a methodology to reflect the changing technology and consider the optimal testing for a clinical condition, rather than a specific gene, to ensure the NHS is receiving the best value from genomic tests across all clinical indications.

The NHS standard contract stipulates that only tests in the National Genomic Test Directory are commissioned and paid for by the NHS and that they must be delivered by a Genomic Laboratory Hub (or their sub-contractors), to the standards set in the service specification. Each NHS Trust has been mapped to a single Genomic Laboratory Hub for the provision of testing.

If you have any questions about the genomic testing available in your area, please contact your local Genomic Laboratory Hub. More information about the Genomic Laboratory Hubs can be found here: https://www.england.nhs.uk/genomics/genomic-laboratory-hubs/.

摘要

国家基因组检测目录为每项临床指征确定了最合适的检测以及应采用的检测方法。国家基因组检测目录载于单独的 excel 文档中，可在以下位置获取：https://www.england.nhs.uk/publication/national-genomic-test-directories/

本检测资格标准文件是国家基因组检测目录的补充文件，规定了在该指征下应考虑接受检测的患者，申请科室列出了预期会申请该检测的临床专科。检测资格标准为哪些患者可能从基因组检测中获益提供了指导。仅当有明确证据表明检测结果极有可能改变患者或其家属的临床管理时，才应申请检测。管理包括确定临床检查；和/或治疗/处理决策或策略；和/或加入国家批准的监测计划；和/或告知和支持生育选择。

为制定国家基因组检测目录和检测标准，NHS England 召集了一个罕见病专家小组。该小组汇集了临床医生、科学家、卫生经济学家、政策专家、公众代表和患者组织。该小组制定了一套方法学，以反映不断变化的技术，并考虑针对临床病症而非特定基因的最佳检测方案，从而确保 NHS 在所有临床指征中从基因组检测中获得最佳价值。

NHS 标准合同规定，只有国家基因组检测目录中的检测才由 NHS 委托并支付费用，且必须由基因组实验室中心(或其分包商)按照服务规范中设定的标准提供。每个 NHS 信托机构均已对应至单一的基因组实验室中心以提供检测。

如果您对所在地区可用的基因组检测有任何疑问，请联系您当地的基因组实验室中心。有关基因组实验室中心的更多信息可在此处找到：https://www.england.nhs.uk/genomics/genomic-Laboratory-hubs/.

Document overview

Clinical Indications

The following elements are presented for each clinical indication:

- **Clinical Indication Name**: name of the clinical indication, preceded by unique clinical indication code.
- **Testing Criteria**: description of the patients who should receive the test.
- **Overlapping Indications**: pointers to other clinical indications with overlapping presentations or genomic targets.
- **Where in Pathway**: guidance as to where the genetic test should usually sit in the patient pathway, particularly with respect to other diagnostic investigations
- **Requesting Specialties**: specialties that will be routinely permitted to request the test

  Requesting specialties have been nationally agreed as appropriate specialties for referrals for testing. The list of requesting specialties is not designed to operate at a very specific level or to limit test requests to just those clinical specialities listed if established alternatives are in place, as pathways will differ across the country, e.g. a specialist with the job title 'paediatric craniofacial surgeon' would potentially be grouped within 'Surgery' or 'Paediatrics'.

  If GLHs receive test requests from clinicians whose role doesn't fall within a single requesting specialty, or whose clinical specialty is not listed for that clinical indication, the GLH can process that test if it is appropriate as per their agreed local pathways, and the eligibility criteria for the clinical indication is being met.
- **Specialist Service Group**: specialist service group that covers the clinical indication. The options are:
  - Core;
  - Cardiology;
  - Audiology;
  - Endocrinology;
  - Ophthalmology;
  - Gastrohepatology;
  - Haematology;
  - Immunology;
  - Inherited cancer;
  - Metabolic;
  - Mitochondrial;
  - Musculoskeletal;
  - Neurology;
  - Renal;
  - Respiratory;
  - Dermatology;
  - Prenatal;

Associated Tests

The associated tests contain information about the tests which routinely constitute the target for the clinical indication. It is expected that all tests listed under a particular clinical indication will be routinely performed, unless there is clear clinical or scientific rationale not to do so.

Information provided includes:

Optimal Family Structure: optimal family structure for testing if relevant relatives are available. The options are:

- Singleton;
- Trio;
- Singleton or Trio;
- Parents only; and
- Other

文档概述

临床适应症

以下为每个临床指征列出的要素：

- 临床指征名称：临床指征的名称，前面附有唯一的临床指征代码。
- 检测标准：应接受该检测的患者的描述。
- 重叠指征：指向其他表现重叠的临床指征的提示，或基因组靶点。
- 在路径中的位置：关于基因检测通常应位于患者路径中何处的指导，特别是相对于其他诊断性检查而言
- 申请专科：常规获准申请该检测的专科

  申请科室已在全国范围内被一致同意为适合转诊进行检测的专科。申请科室清单并非设计用于非常具体的层面运作，也并非在已有既定替代方案的情况下将检测申请仅限于所列的临床专科，因为全国各地的路径会有所不同，例如，职位名称为“儿科颅面外科医生”的专科医生可能被归入“外科”或“儿科”。如果 GLH 收到来自其角色不属于单一申请科室的临床医生、或其临床专科未列入该临床指征的检测申请，只要符合其商定的本地路径且该临床指征的检测资格标准得到满足，GLH 即可处理该检测。
- 专科服务组：涵盖该临床指征的专科服务组。选项为：
  - 核心；
  - 心血管；
  - 听力学；
  - 内分泌；
  - 眼科；
  - 胃肠肝病学；
  - 血液学； 免疫学； 遗传性肿瘤； 代谢。
  - 线粒体；
  - 肌肉骨骼；
  - 神经科；
  - 肾脏；
  - 呼吸系统；
  - 皮肤科；
  - 产前；

相关检测

相关检测包含有关常规构成该临床指征目标的检测的信息。预期特定临床指征下列出的所有检测均将常规执行，除非有明确的临床或科学理由不这样做。

所提供的信息包括：最佳家庭结构：如有相关亲属可用时进行检测的最佳家庭结构。选项为：

– 单例； – 三联体；
– 单例或三联体； – 仅父母；以及– 其他

Scope: the type of variation to be detected. The options are:

- Small variant detection;
- Copy number variant detection to genomewide resolution;
- Copy number variant detection;
- Short tandem repeat analysis;
- Complex variant detection;
- Balanced rearrangement detection;
- Aneuploidy detection;
- Methylation analysis;
- Uniparental disomy detection;
- Identity testing;
- DNA repair defect detection; and
- Other

Target Type: the type of target at which the variants need to be detected. The options are:

- Genomewide;
- Panel of genes or loci;
- Single gene(s); and
- Single interval

Target Name: names of the gene(s)or panel at which the variant type should be detected

Test Method: test method to be used. The options are:

- WGS (Whole Genome Sequencing);
- WES (Whole Exome Sequencing);
- Large panel;
- Medium panel;
- Small panel;
- Single gene sequencing;
- Targeted variant testing;
- STR testing;
- MLPA or equivalent;
- Microarray;
- Common aneuploidy testing;
- Karyotype;
- FISH;
- DNA repair testing;
- Methylation testing;
- Uniparental Disomy (UPD) testing;
- X-inactivation testing;
- Identity testing;
- Microsatellite instability;
- NIPT (Non Invasive Prenatal Testing);
- NIPD (Non Invasive Prenatal Diagnosis);
- Other

Test Ordering

Clinicians wishing to request genomic tests can do so by;

- Requesting the clinical indication (name and unique code of the clinical indication), in instances where the clinical indication to be tested is known
- If the clinician is aware that some of the constituent tests which are offered as part of the clinical indication are not needed, they can specify to the laboratory which constituent tests are required and which aren't.
- As much relevant clinical details as possible should be provided to aid interpretation of results

Clinicians should follow local process to request genomic tests using the most appropriate Clinical Indication code. The Genomic Laboratory Hub will review the test request and relevant clinical information and select the most appropriate constituent test(s) to facilitate the test request. Testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

范围：待检测的变异类型。选项为：

– 小变异检测；

– 拷贝数变异检测至全基因组分辨率；

– 拷贝数变异检测；– 短串联重复序列分析；– 复杂变异检测；

– 平衡重排检测；– 非整倍体检测；– 甲基化分析；

– 单亲二体检测；– 身份检测；

– DNA 修复缺陷检测；以及 – 其他

目标类型
需要检测变异的目标类型。选项为：

– 全基因组范围；

– 基因或基因座组合；– 单基因；以及– 单区间

目标名称

应检测变异类型的基因或 panel 名称检测方法：待使用的检测方法。选项为：

– WGS(全基因组测序);– WES(全外显子组测序);

– 荧光原位杂交（F
– DNA 修复检测；

 大检测板；
– 中等规模 panel;
 小检测板；
 单基因测序；
 靶向变异检测；
– STR 检测；
– MLPA 或等效方法；
 微阵列（基因芯片）；
– 常见非整倍体检测；– 核型分析；

 甲基化检测；
– 单亲二体(UPD)检测；
– X 染色体失活检测；
 身份鉴定检测；
 微卫星不稳定性；
– NIPT(无创产前检测);– NIPD(无创产前诊断);
 其他

检测订购

希望申请基因组检测的临床医生可通过以下方式提出申请；

- 申请临床指征(临床指征的名称和唯一代码)，在以下情况下
  在已知待检测临床指征的情况下
- 如果临床医生知道作为该临床指征一部分提供的某些组成检测
  并不需要，他们可以向实验室指明需要哪些组成检测以及哪些不需要。
- 应提供尽可能多的相关临床细节，以协助结果解读

临床医生应遵循当地流程，使用最合适的临床指征代码申请基因组检测。基因组实验室中心将审查检测申请和相关临床信息，并选择最合适的组成检测以促成该检测申请。检测应针对那些遗传或基因组诊断将指导先证者或家庭管理的患者。

Glossary

- Where the term ‘maternal’ is used this refers to the genetic contribution, from parent to offspring, from an ovum and the term ‘paternal’ refers to the parental contribution from a sperm.
- In the context of **X linked early onset conditions**, where the eligibility criteria relate to a specific sex, this is referring to the sex assigned at birth and hence should be appropriately applied in trans gender individuals.
- Singleton – the patient
- Duo – testing of patient performed simultaneously alongside one of their biological parents
- Trio – testing of patient performed simultaneously alongside both biological parents
- SNVs – Small nucleotide variants
- CNVs – Copy number variants
- ACGS – Association of Clinical Genomic Science (variant classification guidelines)
- ACMG – American College of Medical Genetics (variant classification guidelines)

Find Text in Document

To search the National Genomic Test Directory - Testing Criteria for Rare and Inherited Disease:

1. Press CTRL+F (Windows) or CMD+F (Mac)
2. In text box, enter search term
3. The first match will be highlighted
4. Press Enter or click the arrow keys to navigate between results

术语表

• 使用“母源”一词时，指来自卵子的、从亲代到子代的遗传贡献；使用“父源”一词时，指来自精子的亲代贡献。

• 在**X 连锁早发疾病**的语境中，当检测资格标准涉及特定性别时，这是指出生时指定的性别，因此应适当地应用于跨性别个体。

• 单例 - 患者

• Duo - 患者与其一位生物学亲代同时进行的检测

• Trio - 患者与其双亲同时进行的检测

• SNVs--小核苷酸变异

• CNVs--拷贝数变异

• ACGS - 临床基因组科学协会(变异分类指南)

• ACMG - 美国医学遗传学与基因组学学会(变异分类指南)

在文档中查找文本

搜索国家基因组检测目录 - 罕见与遗传病检测标准：

1. 按 CTRL+F(Windows)或 CMD+F(Mac)
2. 在文本框中，输入搜索词
3. 第一个匹配项将被高亮显示
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Part I. Acutely unwell children

R14 Acutely unwell children with a likely monogenic disorder

Testing Criteria

Acutely unwell children with a likely monogenic disorder

For more detailed guidance for R14 please see http://exeterlaboratory.com/genetics/genome-sequencing/

Where clinical features and/or non genetic investigations are pathognomonic of a single gene disorder, no test is available and molecular testing is required urgently to guide management, R14 may be requested.

Please note that myotonic dystrophy, spinal muscular atrophy (SMA) and Prader Willi syndrome caused by imprinting defects will not be detected by R14 and testing must be requested separately where appropriate

Overlapping indications

- R26 Likely common aneuploidy test should be used first where the cause is considered likely to be a common aneuploidy
- R28 Congenital malformation and dysmorphism syndromes – microarray should be undertaken in parallel where clinically indicated. Where the cause is highly likely to be chromosomal, for example where the clinical features are characteristic of Williams syndrome, then microarray should be undertaken in advance of the R14 test.

Where in Pathway

Following discussion with Clinical Genetics, the child's local management team and the testing laboratory, or in line with locally agreed patient identification criteria

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Multi specialty

Associated Tests

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Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R14.1	Acutely unwell children with a likely monogenic disorder	Trio(Duo or Singleton accepted when necessary)	Small variants and CNVs	Trio gene agnostic or Panel of genes or loci in singletons or duos	Trio gene agnostic or appropriate panels in singletons or duos	WGS

第I.急性不适儿童

R14急性不适儿童伴可能单基因疾病

检测标准

患有疑似单基因疾病的急性不适儿童

有关 R14 的更详细指引，请参见http://exeterlaboratory.com/genetics/genome-sequencing/

当临床特征和/或非遗传学检查为单基因疾病的特征性表现，无可用检测且急需分子检测以指导管理时，可申请 R14。

请注意，由印记缺陷导致的强直性肌营养不良、脊髓性肌萎缩(SMA)和 Prader Willi 综合征不会通过 R14 检出，适当时必须单独申请检测

重叠指征

- R26 当病因被认为可能是常见非整倍体时，应首先使用常见非整倍体检测
  常见非整倍体
- R28 先天畸形和畸形综合征 - 微阵列(基因芯片)应在
  临床有指征时平行进行。当病因极可能为染色体性时，例如临床特征为 Williams 综合征的典型表现，则应在 R14 检测之前进行微阵列(基因芯片)。

通路中的位置

在与临床遗传学团队、患儿当地管理团队和检测实验室讨论后，或符合当地商定的患者识别标准

申请专科

- 临床遗传学

专科服务组

- 多专科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R14.1	急性不适 可能患有 单基因疾病在以下情	三人组（双人或单人 况下被接受： 必要的）	小变异 和拷贝数变异	三人组基因无关检测 或基因检测板 单人中的位点 或双人	三人组基因无关检测或 单人中的适当检测板 或双人	全基因组测序

Part II. Cardiology

R137 Congenital heart disease - microarray

Testing Criteria

Individual with:

- Complex congenital heart disease in a neonate/infant undergoing corrective surgery, in whom other syndromic features may not yet be apparent **AND**
- a syndromic diagnosis may impact surgical decision making.

Test requests must be approved by clinical genetics to proceed.

OR

Tetralogy of Fallot, interrupted aortic arch or truncus arteriosus, or other forms of complex congenital heart disease with cleft palate and / or disorder of calcium homeostasis should be present

Exclusion criteria

Non-syndromic Congenital Heart Disease (CHD) e.g. isolated VSD/ASD outside of the above eligibility criteria should not be tested under R137

Overlapping indications

- R26 Likely common aneuploidy test should be used for patients with coarctation of the aorta and features suggestive of Turner syndrome
- R27 Paediatric disorders – likely monogenic or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations. R27 should NOT be used for isolated CHD, even in the presence of a recurrence in the family.
- R140 Elastin-related phenotypes

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics
- Fetal Medicine
- Paediatrics
- Pathology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R137.1	Genomewide Microarray	Singleton	Genomewide CNVs	Genomewide	Genomewide	Microarray

第二部分II.心脏病学

R137先天性心脏疾病-微阵列(基因芯片)

检测标准

个体具有：

• 接受矫正手术的新生儿/婴儿中的复杂先天性心脏病，其其他综合征特征可能尚未显现**且**

• 综合征性诊断可能影响手术决策。检测申请必须经临床遗传学批准方可进行。

或

应存在法洛四联症、主动脉弓中断或动脉干，或其他形式的复杂先天性心脏病伴腭裂和/或钙稳态紊乱排除标准非综合征性先天性心脏病(CHD)，例如上述检测资格标准之外的孤立性 VSD/ASD，不应在 R137 下进行检测

重叠指征

• R26 对于主动脉缩窄患者，应使用常见非整倍体检测，并且提示特纳综合征的特征

• R27 儿科疾病 - 可能单基因或 R89 超罕见和非典型单基因疾病检测

应用于有先天畸形、畸形特征或其他复杂或综合征表现的个体。R27 不应用于孤立性 CHD，即使家族中存在复发。

• R140 弹性蛋白相关表型

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 心脏病学

• 临床遗传学

• 胎儿医学

• 儿科

• 病理学

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R137.1	全基因组范围微阵列（基因芯片）	单人	全基因组范围拷贝数变异	全基因组范围	全基因组范围	微阵列（基因芯片）

R125 Thoracic aortic aneurysm or dissection

Testing Criteria

1. Thoracic aortic aneurysm* or dissection with onset before age 50, OR
2. Thoracic aortic aneurysm* or dissection with onset before age 60 with a first degree relative with thoracic aortic aneurysm or dissection, OR
3. Clinical features suggestive of Loeys-Dietz syndrome, OR
4. Features of Marfan syndrome giving a systemic Ghent score of ≥7, following assessment by a clinical geneticist or specialist with expertise in aortopathy, OR
5. Any deceased individual with a thoracic aortic aneurysm* or dissection detected at autopsy meeting one of the above criteria and who have relatives who will benefit from cascade testing using a genetic diagnosis will be suitable for post-mortem genetic testing.

*Thoracic aortic aneurysm defined as:

- In children: z score >3for body surface area
- In adults: dilatation >38 mm

Testing should be carried out following assessment in a clinical service specialising in management of patients with aortopathy, including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an aortic genetics MDT

Overlapping Indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R125.1	Thoracic aortic aneurysm or dissection	Singleton	Small variants, CNVs	Panel of genes or loci	Thoracic aortic aneurysm or dissection (700)	WES or Medium Panel

R125胸主动脉动脉瘤或夹层

检测标准

1. 50岁前发病的胸主动脉瘤*或夹层，或
2. 胸主动脉瘤*或夹层，发病年龄在60岁之前，且有一名一级亲属患有胸主动脉瘤或夹层，或
3. 提示Loeys-Dietz综合征的临床特征，或
4. 经临床遗传学家或主动脉病专家评估后，符合Marfan综合征特征且系统性Ghent评分≥7，或
5. 任何已故个体，在尸检时发现胸主动脉瘤*或夹层，且符合上述标准之一，并有其亲属将通过基因诊断受益于级联检测者，适合进行尸检基因检测。

* 胸主动脉瘤定义为：

- 儿童：体表面积 z 评分 >3
- 成人：扩张 >38 mm

检测应在专门管理主动脉病患者的临床服务中评估后进行，包括临床遗传学的支持；在主动脉遗传学MDT讨论后，偶尔可能适合在这些标准之外进行检测

重叠指征

- R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于

患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

- 心脏病学
- 临床遗传学

专科服务组

- 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R125.1	胸主动脉动脉瘤或夹层	单人	小变异，拷贝数变异	基因检测板或基因座	胸主动脉瘤或夹层 (700)	WES或Medium检测板

R127 Long QT syndrome

Testing Criteria

A firm clinical diagnosis of Long QT syndrome, as indicated by:

1. QTc ≥500ms in repeated 12-lead ECGs, OR
2. LQTS risk score ≥3.5 (Schwartz et al, 2011. PMID: 22083145), OR
3. QTc ≥480 ms in repeated 12-lead ECGs AND an unexplained syncopal episode
4. QTc ≥480 ms in repeated 12-lead ECGs AND a history of sudden unexplained death under the age of 60 in a first / second degree relative

A secondary cause for QT prolongation should be excluded prior to testing

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R127.1	Long QT syndrome Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Long QT syndrome (76)	Small panel

R127长QT综合征

检测标准

Long QT 综合征的明确临床诊断，依据为：

1. 重复12导联心电图显示QTc ≥500ms，或
2. LQTS 风险评分 ≥ 3.5(Schwartz 等，2011。PMID: 22083145)，或
3. 重复12导联心电图QTc ≥480 ms且发生不明原因晕厥发作
4. 重复12导联心电图QTc ≥480 ms，且有一级/二级亲属在60岁以下有不明原因猝死史

在检测前应排除QT间期延长的继发性原因

检测应与专家表型评估并行进行，例如在遗传性心脏病门诊(ICC)中，包括临床遗传学的支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 心脏病学

• 临床遗传学

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R127.1	长QT综合征 小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	长QT综合征 (76)	小检测板

R128 Brugada syndrome and cardiac sodium channel disease

Testing Criteria

A firm clinical diagnosis of Brugada syndrome and/or sodium channel disease, as indicated by:

1. Spontaneous type 1 (“coved-type”) ST-segment elevation (characterized by ST-segment elevation ≥2 mm (0.2 mV) in ≥1 right precordial leads (V1–V3) positioned in the 4th, 3rd, or 2nd intercostal space), OR
2. Type 1 ST-segment elevation unmasked using a sodium channel blocker, AND 1 of the following:
   a. Documented VF or polymorphic VT, OR
   b. Syncope of probable arrhythmic cause, OR
   c. A family history of sudden cardiac death at <45 years old with negative autopsy, OR
   d. A coved-type ECGs in family members, OR
   e. Nocturnal agonal respiration OR
   f. Premature atrial arrhythmias at age <30 years

3. Suspicion of sodium channel disease including atrial arrhythmias, sinus node dysfunction, conduction disease and/or QT prolongation, predominantly in children and young people.

NOTE: Clinical evaluation in young probands and cascade testing in families will incorporate assessment for other features of sodium channel disease such as sinus node disease, atrial arrhythmias, conduction disease, dilated cardiomyopathy and long QT syndrome (LQT3 subtype) that may coexist with or supplant type 1, 2 or 3 Brugada ECG patterns. Brugada ECG patterns may be present even in sodium channel genotype negative patients.

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R128.1	Brugada syndrome and cardiac sodium channel disease Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Brugada syndrome (13)	Small panel

R128Brugada综合征和心脏钠通道疾病

检测标准

Brugada综合征和/或钠通道疾病的明确临床诊断，表现为：

1. 自发性1型(“穹隆型”)ST段抬高(特征为≥1个右胸导联(V1-V3)位于第4、第3或第2肋间时ST段抬高≥2 mm(0.2 mV))，或

2. 使用钠通道阻滞剂后显现的1型ST段抬高，且符合以下1项：
   a. 记录到的心室颤动(VF)或多形性室性心动过速(VT)，或
   b. 可能由心律失常引起的晕厥，或
   c. 有<45岁心源性猝死家族史且尸检阴性,或
   d. 家族成员中出现穹隆型心电图，或
   e. 夜间濒死呼吸 OR
   f. 30岁前发生的房性心律失常

3. 怀疑钠通道疾病，包括房性心律失常、窦房结功能障碍、传导疾病和/或QT延长，主要见于儿童和年轻人。

注：对年轻先证者的临床评估和家族的级联检测将包括对钠通道疾病其他特征的评估，如窦房结疾病、房性心律失常、传导疾病、扩张型心肌病和长QT综合征(LQT3亚型)，这些特征可能与1型、2型或3型Brugada心电图模式共存或取代之。即使钠通道基因型阴性患者也可能出现Brugada心电图模式。检测应与专家表型评估并行进行，例如在遗传性心脏病门诊(ICC)进行，包括临床遗传学的支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的人群。

通路中的位置

申请专科

• 心脏病学
• 临床遗传学

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R128.1	Brugada综合征和心脏钠通道病 小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	Brugada综合征(13)	小检测板

R129 Catecholaminergic polymorphic VT

Testing Criteria

A firm clinical diagnosis of CPVT based on one of the following:

1. A structurally normal heart, normal ECG, and unexplained exercise or catecholamine-induced bidirectional VT or polymorphic ventricular premature beats or VT/VF in an individual under 40 years of age, OR
2. A patient with a structurally normal heart who manifests exercise-induced premature ventricular contractions (PVCs) or bidirectional/polymorphic VT/VF, with a positive family history of CPVT, where a symptomatic family member is unavailable for testing, OR
3. A structurally normal heart and coronary arteries, normal ECG, and unexplained exercise or catecholamine-induced bidirectional VT or polymorphic ventricular premature beats or VT/VF in an individual over 40 years of age

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R129.1	Catecholaminergic polymorphic VT Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Catecholaminergic polymorphic VT (214)	Small panel

R129儿茶酚胺敏感性多形性VT

检测标准

基于以下任一项对CPVT作出明确的临床诊断：

1. 心脏结构正常、心电图正常，且40岁以下个体出现不明原因的运动或儿茶酚胺诱导的双向性VT或多形性室性早搏或VT/VF，或
2. 心脏结构正常的患者，表现为运动诱发的室性早搏(PVCs)或双向性/多形性VT/VF，且有CPVT阳性家族史，但有症状的家庭成员无法进行检测，或
3. 心脏和冠状动脉结构正常、心电图正常，且40岁以上个体出现不明原因的运动或儿茶酚胺诱导的双向性VT或多形性室性早搏或VT/VF

检测应与专家表型评估并行进行，例如在遗传性心脏病门诊(ICC)中，包括临床遗传学的支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 心脏病学
• 临床遗传学

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R129.1	儿茶酚胺敏感性多形性室性心动过速小panel	单人	小变异，拷贝数变异	基因检测板或基因座	儿茶酚胺敏感性多形性室性心动过速 (214)	小检测板

R130 Short QT syndrome

Testing Criteria

A firm clinical diagnosis of Short QT syndrome, as indicated by:

1. A QTc ≤330 ms, OR
2. A QTc <360 ms, AND one or more of the following:
    a. Family history of SQTS,
    b. Family history of sudden death at age ≤40
    c. Survival of a VT/VF episode in the absence of heart disease

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R130.1	Short QT syndrome Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Short QT syndrome (224)	Small panel

R130短QT综合征

检测标准

短QT综合征的明确临床诊断，表现为：

1. QTc ≤330 ms，或
2. QTc <360 ms,并且满足以下一项或多项:
    a. SQTS家族史，
    b. 家族史中年龄≤40岁发生猝死
    c. 无心脏病情况下VT/VF发作的存活

检测应与专家表型评估并行进行，例如在遗传性心脏病门诊(ICC)中，包括临床遗传学的支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 心脏病学
• 临床遗传学

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R130.1	短QT综合征 小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	短QT综合征 (224)	小检测板

R131 Hypertrophic cardiomyopathy

Testing Criteria

A firm clinical diagnosis of hypertrophic cardiomyopathy as indicated by:

1. An adult with wall thickness ≥15 mm in one or more LV myocardial segments, that is NOT explained solely by loading conditions (principally hypertension), with age of onset below 60
2. A child under the age of 18 with LV wall thickness more than two standard deviations greater than the predicted mean (z-score >2, where a z-score is defined as the number of standard deviations from the population mean)
3. Otherwise unexplained increased LV wall thickness ≥13 mm in one or more LV myocardial segments, in a patient with a first degree relative with unequivocal disease (LVH ≥15 mm), where a family member with unequivocal disease is unavailable for testing
4. A deceased individual with pathologically confirmed HCM for post-mortem DNA analysis

Genetic testing is recommended in patients meeting the above criteria who have relatives who will benefit from cascade testing using a genetic diagnosis.

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT.

Overlapping indications

R135 Paediatric or syndromic cardiomyopathy should be used where atypical features suggest a broader range of genes should be tested. All patients tested under R135, must meet the eligibility criteria for R135.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R131.1	Hypertrophic cardiomyopathy WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Hypertrophic cardiomyopathy - teen and adult (49)	WES or Medium Panel

R131肥厚型心肌病

检测标准

肥厚型心肌病的明确临床诊断，表现为：

1. 成人一个或多个LV心肌节段壁厚度≥15 mm，且不能仅由负荷条件(主要是高血压)解释，发病年龄低于60岁
2. 18岁以下儿童LV壁厚度超过预测均值两个标准差以上(z-score >2，其中z-score定义为距人群均值的标准差数)
3. 在其他方面无法解释的一个或多个LV心肌节段LV壁厚度增加≥13 mm，患者有一名一级亲属患有明确疾病(LVH ≥15 mm)，且有明确疾病的家庭成员无法进行检测
4. 已故个体经病理学确认HCM，用于尸检DNA分析

建议对符合上述标准且有亲属将通过基因诊断受益于级联检测的患者进行基因检测。检测应与专家表型评估并行进行，例如在遗传性心脏病门诊(ICC)中，包括临床遗传学的支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测。

重叠指征

R135 儿科或综合征性心肌病应在非典型特征提示应检测更广泛基因时使用。所有在R135下检测的患者必须符合检测资格标准

通路中的位置

申请专科

• 心脏病学
• 临床遗传学

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R131.1	肥厚型心肌病 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	肥厚型心肌病 - 青少年和成人 (49)	WES或Medium检测板

R132 Dilated and arrhythmogenic cardiomyopathy

Testing Criteria

A firm clinical diagnosis of dilated cardiomyopathy (DCM) or arrhythmogenic cardiomyopathy (ACM) as indicated by:

1. Left ventricular end diastolic diameter (LVEDD) greater than 2 standard deviations, AND/OR
   a. Reduced ejection fraction (EF) to less than 45%, adjusted for age and sex, AND
   b. Age of onset below 65 years

OR

2. Left and/or biventricular cardiomyopathy associated with variable degrees of myocardial dysfunction and/or myocardial fibrosis PLUS ventricular arrhythmias (including prior cardiac arrest) following exclusion of other aetiologies including inflammatory disorders

OR

3. A deceased individual with pathologically confirmed DCM or ACM and age of onset below 65 years suitable for post-mortem DNA analysis.

OR

4. Patient with DCM or ACM at any age if they have a first degree relative with confirmed diagnosis of DCM or ACM

Genetic testing is recommended for patients meeting the above criteria with:

1. Relatives who will benefit from cascade testing using genetic diagnosis, AND/OR
2. Features suggesting an increased risk of sudden death, including conduction defects, atrial arrhythmia or family history of sudden death

Patients with ventricular dilatation secondary to coronary artery disease or pressure/volume overload should NOT be tested.

Patients with DCM due to other precipitants (such as myocarditis, alcohol, peripartum, chemotherapy) should only be tested following consultation with an expert

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT

Overlapping indications

- R135 Paediatric or syndromic cardiomyopathy should be used where atypical features suggest a broader range of genes should be tested

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R132.1	Dilated and arrhythmogenic cardiomyopathy	Singleton	Small variants, CNVs	Panel of genes or loci	Dilated cardiomyopathy - teen and adult (652)	WES or Medium Panel

R132扩张型和致心律失常性心肌病

检测标准

扩张型心肌病(DCM)或致心律失常性心肌病(ACM)的明确临床诊断，表现为
由以下情况提示：

1. 左心室舒张末期内径(LVEDD)大于2个标准差，和/或
   a.射血分数(EF)降低至小于45%，按年龄和性别调整，且 b.发病年龄低于65岁

或

2. 左心室和/或双心室心肌病，伴有不同程度的心肌功能障碍和/或心肌纤维化，加上室性心律失常(包括既往心脏骤停)，在排除其他病因包括炎症性疾病后

或

3. 一名经病理学确诊为DCM或ACM、发病年龄低于65岁、适合进行死后DNA分析的已故个体。

或

4. 任何年龄的DCM或ACM患者，若其一级亲属已确诊DCM或ACM。

建议对符合上述标准的以下患者进行基因检测：

1. 将受益于利用基因诊断进行级联检测的亲属，和/或
2. 提示猝死风险增加的特征，包括传导缺陷、房性心律失常或猝死家族史。

继发于冠状动脉疾病或压力/容量负荷过重的心室扩张患者不应接受检测。由其他诱因(如心肌炎、酒精、围产期、化疗)所致DCM的患者仅应在咨询专家后接受检测。检测应与专家表型评估并行进行，例如在遗传性心脏病门诊(ICC)进行，包括临床遗传学的支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测

重叠指征

• R135 儿童期或综合征性心肌病应用于非典型特征提示
应检测更广泛的基因范围

通路中的位置

申请专科

• 心脏病学
• 临床遗传学

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R132.1	扩张型和致心律失常性心肌病	单人	小变异，拷贝数变异	基因检测板或基因座	扩张型心肌病 - 青少年和成人 (652)	WES或Medium检测板

R391 Barth syndrome

Testing Criteria

Clear clinical and biochemical diagnosis of Barth syndrome in a male patient:

1. Some or all of cardiomyopathy, neutropenia, skeletal myopathy, prepubertal growth delay, distinctive facial features, and history of unexplained recurrent miscarriage or stillbirths or sudden death in the family, AND
2. Positive cardiolipin result (MLCL/CL ratio) where available; (patients may also have raised 3MGA)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a consultant in cardiology, neonatology, neurology or paediatrics, or following clinical assessment as part of the Barth Syndrome highly specialised service

Requesting Specialties

- Cardiology
- Clinical Genetics
- Neonatology
- Neurology
- Paediatrics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R391.1	TAZ Single gene sequencing	Singleton	Small variants	Single gene(s)	TAZ (1308)	Single gene sequencing >=10 amplicons

R391Barth综合征

检测标准

男性患者 Barth 综合征的明确临床和生化诊断：

1. 心肌病、中性粒细胞减少、骨骼肌病、青春期前生长迟缓、特征性
   面部特征，以及不明原因反复流产或死胎或猝死史中的部分或全部表现，
   家族，AND
2. 心磷脂结果阳性(MLCL/CL比值)(如可获得);(患者也可能有3MGA升高)检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

通路中的位置

在心脏病学、新生儿学、神经病学或儿科顾问医师评估后就诊时，或作为Barth综合征高度专业化服务的一部分进行临床评估后。

申请专科

- 心脏病学
- 临床遗传学
- 新生儿科
- 神经科
- 儿科

专科服务组

- 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R391.1	TAZ单基因测序	单人	小变异	单基因	TAZ (1308)	单基因测序 >=10扩增子

R133 Arrhythmogenic right ventricular cardiomyopathy

Testing Criteria

A firm clinical diagnosis of arrhythmogenic right ventricular cardiomyopathy as indicated by:

1. An individual meeting a definite diagnosis according to the Modified Task Force Criteria (Marcus et al 2010; PMID: 20172912), with age of onset below age 50 OR
2. A deceased individual with pathologically confirmed ARVC and relatives who will benefit from cascade testing using genetic diagnosis. OR
3. Identification of a pathogenic or likely pathogenic variant in an ARVC associated gene would complete diagnostic task force criteria for ARVC.

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT

Overlapping indications

- R132 Dilated cardiomyopathy should be used if disease is left-sided or biventricular, or there is phenotypic overlap with dilated cardiomyopathy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R133.1	Arrhythmogenic right ventricular cardiomyopathy Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Arrhythmogenic cardiomyopathy (134)	Small panel

R133致心律失常性右心室心肌病

检测标准

明确的致心律失常性右心室心肌病临床诊断，表现为：

1. 符合修订版特别工作组标准(Marcus等，2010;PMID: 20172912)的明确诊断个体，且发病年龄低于50岁，或
2. 一名经病理学确诊为ARVC的已故个体，且其亲属将受益于利用遗传诊断进行的级联检测。或
3. 在ARVC相关基因中鉴定出致病变异或可能致病变异将完善ARVC的诊断特别工作组标准。

检测应与专家表型评估同时进行，例如在遗传性心脏病门诊(ICC)进行，包括临床遗传学的支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测。

重叠指征

- R132 扩张型心肌病应用于疾病为左侧或双心室性，或存在与扩张型心肌病存在表型重叠

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 心脏病学
- 临床遗传学

专科服务组

- 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R133.1	致心律失常性右心室心肌病小panel	单人	小变异，拷贝数变异	基因检测板或基因座	致心律失常性心肌病 (134)	小检测板

R135 Paediatric or syndromic cardiomyopathy

Testing Criteria

1. Cardiomyopathy of onset <12 years with no non-genetic explanation, OR
2. Individuals of any age with cardiomyopathy as their primary clinical presentation, where there is also dysmorphism or other feature(s) suggestive of a syndromic cause such as a Rasopathy.

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC) or specialist paediatric cardiology service, including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT.

Testing Criteria for Semi-Rapid Testing

- Acutely unwell children where monogenic paediatric cardiomyopathy is considered highly likely to be the primary cause of the phenotype in the patient.

- Cases should meet the standard eligibility criteria for R135, AND

- Where testing will provide an immediate change to treatment or clinical management for the patient eg. To inform a decision about cardiac transplant, therapeutic intervention or prenatal testing for an ongoing at risk pregnancy.

- The patient is either not eligible for the R14 pathway or Rapid R135 is considered to be the more appropriate test.

Note: Cases where cardiomyopathy is part of a more complex presentation or the clinical presentation is highly suggestive of a fully penetrant monogenic disorder should be considered for R14 instead of rapid R135.

Overlapping indications

- In individuals where cardiomyopathy is one of multiple features of a likely multisystem disorder R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used to enable testing of broader targets and familial testing where available
- Specific cardiomyopathy categories R131, R132 or R133 should be used where features are typical of non-syndromic hypertrophic, dilated or arrhythmogenic cardiomyopathy in individuals over the age of 12

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Where in Pathway for Semi-Rapid Testing

At presentation following clinically relevant, rapidly available investigations. All cases must be agreed in advance with the testing laboratory.

Requesting Specialties

- Cardiology
- Clinical Genetics

Requesting Specialties for Semi-Rapid Testing

- Clinical Genetics
- Cardiology
- Neonatology

Specialist Service Group

- Cardiology

Associated Tests (see next page)

R135.3 is only for semi urgent testing

R135儿童期或综合征性心肌病

检测标准

1. 12岁前发病且无其他非遗传学解释的心肌病，或
2. 任何年龄以心肌病为主要临床表现的个体，同时存在畸形或其他提示综合征性病因(如Rasopathy)的特征。

检测应与专家表型评估同时进行，例如在遗传性心脏病门诊(ICC)或专科儿科心脏病学服务中进行，包括临床遗传学的支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测。

半快速检测标准

- 急性病重儿童，其中单基因儿科心肌病被认为极可能是患者表型的原发原因。

- 病例应符合 R135 的标准资格标准，并且

- 检测将立即改变患者治疗或临床管理的情况，例如为心脏移植、治疗干预或对持续高危妊娠进行产前检测的决策提供信息。

- 患者不符合R14路径的资格，或快速R135被认为是更合适的检测。

注：心肌病为更复杂表现的一部分，或临床表现高度提示完全外显的单基因疾病的病例，应考虑R14而非快速R135。

重叠指征

• 在心肌病为可能的多系统疾病多个特征之一的个体中，应使用R27儿科疾病或R89超罕见和非典型单基因疾病检测，以便在可获得时对更广泛的目标和家族进行检测。

• 在特征典型的情况下，应使用特定的心肌病类别 R131、R132 或 R133

12 岁以上个体的非综合征型肥厚型、扩张型或致心律失常性心肌病检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

通路中的位置

半快速检测路径中

在临床相关、可快速获得的检查后就诊时。所有病例必须事先与检测实验室达成一致。

• 心脏病学
• 临床遗传学

申请专科进行半快速检测

• 临床遗传学
• 心脏病学
• 新生儿科

专科服务组

• 心脏病学

相关检测（见下页）R135.3 仅用于半紧急检测

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R135.2	Paediatric or syndromic cardiomyopathy	Trio or Singleton	Small variants, CNVs	Panel of genes or loci	Cardiomyopathies - including childhood onset (749)	WGS
R135.3	Paediatric or syndromic cardiomyopathy	Trio	Small variants, CNVs	Panel of genes or loci	Cardiomyopathies - including childhood onset (749)	WES

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R135.2	儿科或综合征性心肌病	三人组或单人小检测板	变异，拷贝数变异	基因检测板或基因座	心肌病 - 包括儿童期发病 (749)	全基因组测序
R135.3	儿科或综合征性心肌病	三人组	小检测板变异，拷贝数变异	基因检测板或基因座	心肌病 - 包括儿童期发病 (749)	全外显子组测序

R136 Primary lymphoedema

Testing Criteria

Primary lymphoedema with or without syndromic manifestations, with no known explanation

If in doubt whether testing is indicated, refer for specialist investigation to a specialist clinic such as those based in Derby or at St Georges Hospital in London

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Other

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R136.1	Primary lymphoedema WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Primary lymphoedema (65)	WES or Medium Panel

R136原发性淋巴水肿

检测标准

原发性淋巴水肿，伴或不伴综合征表现，无已知病因

如对是否有检测指征存有疑问，请转诊至专科门诊进行专科评估，例如位于Derby或伦敦St Georges Hospital的专科门诊

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 其他

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R136.1	原发性淋巴水肿全外显子组测序或中等 panel	单人	小变异，拷贝数变异	基因检测板或基因座	原发性淋巴水肿 (65)	WES或Medium检测板

R138 Sudden unexplained death or survivors of a cardiac event

Testing Criteria

1. Sudden death with normal post-mortem below the age of 40, OR
2. Sudden death with normal post-mortem below the age of 60, with a family history of unexplained sudden death under the age of 40 in a first / second degree relative (in whom no post-mortem was carried out), OR
3. Sudden death with normal post-mortem below the age of 60, with a family history of unexplained sudden death under the age of 60 in a first / second degree relative (where the relative also had a normal post-mortem)

Where available, the post-mortem should include assessment by an expert in cardiac autopsy.

Where a cause can be identified via post-mortem or through clinical assessment of surviving relatives, the appropriate specific Clinical Indication for testing should be used.

Testing should be carried out in parallel with assessment of surviving relatives in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT or an opinion from an expert in cardiac autopsy.

Survivors of proven cardiac arrest (idiopathic ventricular fibrillation) with:

1. no phenotype detectable on comprehensive evaluation including coronary assessment, cardiac imaging and ECG provocation testing (idiopathic ventricular fibrillation) AND
2. under the age of 45.

Testing should be carried out in parallel with expert phenotypic assessment, for example in an Inherited Cardiac Clinic (ICC), including support from clinical genetics; testing may occasionally be appropriate outside these criteria following discussion in an ICC MDT.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family. for cardiac arrest survivors or relatives

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R138.1	Sudden unexplained death or survivors of a cardiac event WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Sudden cardiac death (841)	WES or Medium Panel

R138不明原因猝死或心脏事件的幸存者

检测标准

1. 40岁以下猝死且尸检正常，或
2. 60岁以下尸检正常的猝死，且一级/二级亲属中有40岁以下不明原因猝死的家族史(该亲属未进行尸检)，或
3. 60岁以下尸检正常的猝死，且一级/二级亲属中有60岁以下不明原因猝死的家族史(该亲属尸检亦正常)

如条件允许，尸检应包括由心脏尸检专家进行的评估。

如可通过尸检或通过对存活亲属的临床评估确定病因，则应使用相应的特定临床指征进行检测。检测应与遗传性心脏病门诊(ICC)中对存活亲属的评估同步进行，包括临床遗传学支持；在ICC MDT讨论后或经心脏尸检专家提供意见后，偶尔可能适合在这些标准之外进行检测。

经证实的心脏骤停(特发性心室颤动)幸存者，且：1. 全面评估(包括冠状动脉评估、心脏影像学)

和ECG激发试验均未检出表型(特发性心室颤动)，且2. 年龄在45岁以下。

检测应与专家表型评估同步进行，例如在遗传性心脏病门诊(ICC)中进行，包括临床遗传学支持；在ICC MDT讨论后，偶尔可能适合在这些标准之外进行检测。

检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。适用于心脏骤停幸存者或亲属

通路中的位置

申请专科

• 心脏病学

• 临床遗传学

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R138.1	猝死 不明原因死亡 或心脏事件幸存者 WES 或中等 panel	单人	小变异， 拷贝数变异	基因检测板或 基因座	心源性猝死 (841)	WES或Medium 检测板

R328 Progressive cardiac conduction disease

Testing Criteria

Unexplained progressive conduction abnormalities with onset before age 50 years, with a structurally normal heart and in the absence of a skeletal myopathy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R328.1	Progressive cardiac conduction disease WES or small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Progressive cardiac conduction disease (506)	WES or Small Panel

R328进行性心脏传导疾病

检测标准

50岁前发病的不明原因进行性传导异常，心脏结构正常且无骨骼肌病

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 心脏病学

• 临床遗传学

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R328.1	进行性心脏传导疾病 WES 或小 panel	单人	小变异，拷贝数变异	基因检测板或基因座	进行性心脏传导疾病 (506)	WES或Small检测板

R384 Generalised arterial calcification in infancy

Testing Criteria

Generalised arterial calcification with onset in the neonatal period

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neonatology

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R384.1	Generalised arterial calcification in infancy	Singleton	Small variants	Small panel	ABCC6; ENPP1 (1337)	Small panel

R384婴儿期全身性动脉钙化

检测标准

新生儿期发病的全身性动脉钙化

通路中的位置

就诊时

申请专科

• 临床遗传学

• 新生儿科

专科服务组

• 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R384.1	全身性动脉钙化 婴儿期	单人	小变异	小检测板	ABCC6；ENPP1 (1337)	小检测板

R140 Elastin-related phenotypes

Testing Criteria

1. Congenital heart disease of a type associated with Elastin variants, with an autosomal dominant pattern of inheritance in at least 3 family members, OR
2. Supravalvular aortic stenosis characteristic of Elastin variants

Overlapping indications

- R28 Congenital malformation and dysmorphism syndromes – microarray only should be used for patients with clinical features strongly suggestive of Williams syndrome
- R27 Paediatric disorders test should be used for individuals with syndromic forms of cutis laxa. Requests must meet the eligibility criteria for R27.
- R125 Thoracic aortic aneurysm or dissection test should be used for individuals with primarily aortic/large arterial involvement, with some features of cutis laxa. Requests must meet the eligibility criteria for R125.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R140.1	ELN Single gene sequencing	Singleton	Small variants	Single gene(s)	ELN (1322)	Single gene sequencing >=10 amplicons

R140弹性蛋白相关表型

检测标准

1. 与Elastin变异相关的先天性心脏病，呈常染色体显性遗传模式
至少3名家庭成员的遗传方式，或
2. 主动脉瓣上狭窄，为弹性蛋白变异的特征

重叠指征

- R28 先天性畸形和畸形综合征 - 仅微阵列(基因芯片)应用于
具有强烈提示Williams综合征临床特征的患者
- R27 儿科疾病检测应用于具有综合征型皮肤松弛症的个体。
请求必须符合 R27 的资格标准。
- R125 胸主动脉瘤或夹层检测应用于主要以
主动脉/大动脉受累、伴有一些皮肤松弛症特征的个体。申请必须符合R125的检测资格标准。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 心脏病学
- 临床遗传学

专科服务组

- 心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R140.1	ELN单基因测序	单人	小变异	单基因	ELN(1322)	单基因测序 >=10扩增子

R441 Unexplained death in infancy and sudden unexplained death in childhood

Testing Criteria

1. Sudden death in child less than 18 years that remains unexplained after the standard investigation protocols, Joint Agency Response (JAR) review of circumstances of death and post-mortem **AND**
2. Confirmation from requesting clinician that 1. is fulfilled **AND**
    - DNA is available from proband and both biological parents for trio WGS analysis OR
    - Where only one parent, or neither parents, are available for testing then testing the deceased infant/child may proceed in exceptional circumstances. A discussion is required between the clinical team involved and the testing laboratory to consider the most appropriate testing approach and how to proceed.

Test Exclusion; Testing should **not** be performed where the likelihood of a monogenic disorder is low, for example where the available evidence supports a non-genetic cause of death (e.g. severe infection, suspicious death/homicide investigation).

Where in Pathway

Statutory Child Death Review Process for all unexpected deaths includes Joint Agency Response (JAR) review of medical and family history, and circumstances of death.

After standard SIDS/SUDC protocol including JAR review and post-mortem have been completed. Following specialist MDT discussion of patients that may be suitable for WGS (including e.g. pathology, designated doctor for child deaths, clinical genetics as appropriate). Consent will need to be obtained from family.

Requesting Specialties

- Clinical Genetics (in liaison with designated doctor for child deaths)
- Paediatrics (in liaison with designated doctor for child deaths)

Specialist Service Group

- Multi specialty

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R441.1	Unexplained death in infancy and sudden unexplained death in childhood WGS	Trio or duo	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Unexplained death in infancy and sudden unexplained death in childhood (1220)	WGS

R441不明原因死亡于婴儿期及突发不明原因死亡于儿童期

检测标准

1. 18岁以下儿童突发死亡，经标准检查后仍原因不明
方案、联合机构响应(JAR)对死亡情况及尸检的审查**和**
2. 申请临床医生确认已满足第1项**且**
o 可获取先证者及双亲生物学父母的DNA用于trio WGS分析或 o 当仅有一方亲本或无亲本可供检测时，对deceased
婴儿/儿童可在特殊情况下继续进行检测。需要相关临床团队与检测实验室进行讨论，以考虑最合适的检测方法及如何进行。

检测排除；在单基因疾病可能性低的情况下，**不**应进行检测，例如现有证据支持非遗传性死因(如严重感染、可疑死亡/凶杀调查)。

通路中的位置

对所有意外死亡的法定儿童死亡审查流程包括联合机构响应(JAR)对病史和家族史以及死亡情况的审查。

在完成标准SIDS/SUDC方案(包括JAR审查和尸检)之后。经专科MDT讨论可能适合WGS的患者后(包括如病理学、儿童死亡指定医生、临床遗传学等酌情参与)。需获得家属知情同意。

申请专科

• 临床遗传学(与儿童死亡指定医生联络)

• 儿科(与指定的儿童死亡医生联络)

专科服务组

• 多专科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R441.1	不明原因死亡在婴儿期和猝然不明原因死亡在儿童期WGS中	三人组或双人组	外显子水平CNVs，小变异，短串联重复序	基因检测板或基因座	婴儿期不明原因死亡以及不明原因猝死儿童期（1220）	全基因组测序

R454 Mavacamten for treating symptomatic obstructive hypertrophic cardiomyopathy

Testing Criteria

Testing is available to patients with:

1. symptomatic obstructive hypertrophic cardiomyopathy who have a New York Heart Association class of 2 to 3 **AND**
2. are eligible for treatment with mavacamten in line with NICE TA 913 (where mavacamten is an add on to individually optimised standard care that includes beta blockers, non-dihydropyridine calcium-channel blockers or disopyramide, unless these are contraindicated).

Where in Pathway

At prescribing decision

Requests for this test will only be accepted from centres that are commissioned to prescribe Mavacamten.

Requesting Specialties

- Cardiology

Specialist Service Group

Cardiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R454.1	Mavacamten for treating symptomatic obstructive hypertrophic cardiomyopathy	Singleton	*2, *3 and *17 alleles	Single gene	CYP2C19	Targeted variant testing

R454Mavacamten用于治疗有症状的梗阻性肥厚型心肌病

检测标准

检测适用于以下患者：

1. 有症状的梗阻性肥厚型心肌病，纽约心脏协会分级为2 至 3 的**和**
2. 符合NICE TA 913标准可使用mavacamten治疗(其中mavacamten是在个体化优化标准治疗基础上的附加治疗，标准治疗包括β受体阻滞剂、非二氢吡啶类钙通道阻滞剂或丙吡胺，除非存在禁忌)。

通路中的位置

在处方决策时

该检测申请仅接受来自获准处方Mavacamten的中心。

申请专科

- 心脏病学

专科服务组

心脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R454.1	Mavacamten用于治疗有症状的梗阻性肥厚性心肌病	单人	*2、*3 和 *17等位基因	单基因	CYP2C19	靶向变异检测

Part III. Developmental disorders

R26 Likely common aneuploidy

Testing Criteria

Clinical features strongly suggestive of trisomy 13, 18 or 21, Turner syndrome or other sex chromosome aneuploidy in the postnatal setting

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management

Overlapping indications

- R265 Chromosomal mosaicism – karyotype,
- R314 Ambiguous genitalia; plus any other follow-on tests should be considered in cases with a negative result
- R401 Common aneuploidy testing - prenatal test should be used for prenatal testing

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Community Paediatrics
- Neonatology
- Paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R26.1	Genomewide Common aneuploidy testing - postnatal	Singleton	Aneuploidy	Genomewide	Genomewide	Common aneuploidy testing

第三部分III.发育性疾病

R26可能常见非整倍体

检测标准

出生后临床特征强烈提示13、18或21三体、Turner综合征或其他性染色体非整倍体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导管理的患者

重叠指征

- R265 染色体嵌合体 - 核型，
- R314 生殖器性别不明；另在结果为阴性时应考虑其他后续检测结果
- R401 常见非整倍体检测--产前检测应使用产前检测

通路中的位置

申请专科

- 临床遗传学
- 社区儿科
- 新生儿科
- 儿科

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R26.1	全基因组范围常见非整倍体检测--出生后	单人	非整倍体	全基因组范围	全基因组范围	常见非整倍体检测

R27 Paediatric disorders

Testing Criteria

- Congenital malformations and/or dysmorphism highly suggestive of an underlying monogenic disorder where targeted genetic testing is not possible.
- Unexplained moderate/severe/profound global developmental delay or unexplained moderate/severe/profound intellectual disability, and where clinical features are highly suggestive of an underlying monogenic disorder requiring sequencing and targeted genetic testing is not possible.
- Craniofacial dysmorphism in combination with additional issues with health or development suggestive of a single genomic explanation, e.g. intellectual disability, congenital malformation, organ dysfunction.
- Syndromic overgrowth or overgrowth in combination with intellectual disability or developmental delay.
- Adults with congenital malformation and dysmorphism syndromes, however the clinical utility of testing should be made clear on the request form e.g. to inform a clinical management decision or reproductive choice.
- Fetus from a demised/non-continued pregnancy, with multiple major structural abnormalities detected on fetal ultrasound or post-mortem examination and where a monogenic malformation disorder is considered highly likely
- Unexplained epilepsy with clinical suspicion of a monogenic cause including onset under 2 years, OR clinical features suggestive of specific genetic epilepsy, for example Dravet syndrome.

Exclusion criteria

- Isolated Congenital Heart Disease and other isolated congenital malformations where the likelihood of a monogenic disorder is low are not eligible for testing under this indication.
- Isolated craniofacial dysmorphism is not an indication for testing; exceptions to this can only be made following multidisciplinary discussion with clinical genetics.

R28 microarray testing is not a requirement prior to R27 being initiated in patients with a possible monogenic cause of a syndromic paediatric disorder in whom there are no recognisable features of a specific chromosome disorder (eg 22q11 deletion syndrome).

Overlapping indications

- R14 Acutely unwell infants with a likely monogenic disorder test should be used instead where relevant where a rapid result is required and in children with onset under the age of 12 months with unexplained epilepsy.
- R412 Fetal anomalies with a likely genetic cause – non urgent can be used in a fetus where insufficient DNA is available for R27
- R28 Congenital malformation and dysmorphism syndromes – microarray, should be considered prior to R27 in patients suspected of having a recognisable chromosomal disorder e.g. 22q11 deletion syndrome.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following discussion with Consultant in Clinical Genetics or another relevant subspecialist approved by Genomic Laboratory Hub

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Paediatric neurology
- Paediatrics
- Community Paediatrics
- Psychiatry

R27儿科疾病

检测标准

• 先天性畸形和/或畸形特征高度提示潜在单基因疾病，且无法进行靶向遗传检测。

• 不明原因的中度/重度/极重度全面发育迟缓或不明原因的中度/重度/极重度智力障碍，且临床特征高度提示需要测序的潜在单基因疾病，且无法进行靶向遗传检测。

• 颅面畸形合并其他健康或发育问题，提示单一基因组解释，例如智力障碍、先天性畸形、器官功能障碍。

• 综合征性过度生长或过度生长合并智力障碍或发育延迟。

• 患有先天性畸形和畸形综合征的成人，但检测的临床效用应在申请表中明确说明，例如用于指导临床管理决策或生殖选择。

• 已死亡/未继续妊娠的胎儿，胎儿超声或尸检发现多发重大结构异常，且认为单基因畸形疾病可能性极高

• 不明原因癫痫，临床怀疑单基因病因，包括2岁以下起病，或临床特征提示特定遗传性癫痫，例如Dravet综合征。

排除标准

• 孤立性先天性心脏病及其他孤立性先天性畸形，单基因疾病可能性低者，不符合本指征下的检测条件。

• 孤立性颅面畸形不是检测指征；例外情况仅可在与临床遗传学多学科讨论后作出。

R28 微阵列(基因芯片)检测并非在具有可能的单基因病因、且无特定染色体疾病(如 22q11 缺失综合征)可识别特征的综合征性儿科疾病患者中启动 R27 之前的要求。

重叠指征

• 对于可能为单基因疾病的急性不适婴儿，在相关情况下应改用 R14 检测在需要快速结果时，以及对于发病年龄在 12 月龄以下且患有不明原因癫痫的儿童。

• R412 具有可能遗传原因的胎儿异常 - 非紧急情况下可用于 DNA 不足以进行 R27 的胎儿

• R28 先天畸形和畸形综合征 - 微阵列(基因芯片)，对于疑似患有可识别染色体疾病(如 22q11 缺失综合征)的患者，应考虑在 R27 之前进行。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，经与临床遗传学顾问或经基因组实验室中心批准的其他相关亚专科医生讨论后

申请专科

• 临床遗传学
• 代谢医学
• 小儿神经科
• 儿科
• 社区儿科
• 精神病学

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R27.3	Paediatric disorders	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Paediatric disorders (486)	WGS

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R27.3	儿科疾病 三人组或单人		外显子水平 CNV，小变异、STRs	基因检测板或基因座	儿科疾病（486）	全基因组测序

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R28 Congenital malformation and dysmorphism syndromes – microarray only

Testing Criteria

Clinical features highly suggestive of a chromosomal cause, for example individuals with features characteristic of Williams syndrome

Where possible, the chromosomal disorder suspected should be specified on the test request form.

R28 microarray testing is not a requirement prior to R27 being initiated in patients with a possible monogenic cause of a syndromic paediatric disorder in whom there are no recognisable features of a specific chromosome disorder (e.g. 22q11 deletion syndrome).

Overlapping indications

- R27 Paediatric disorders test should be used instead where the likelihood of a chromosomal cause is lower
- R26 Likely common aneuploidy test should be used where clinical features are strongly suggestive of trisomy 13, 18 or 21, Turner syndrome or other sex chromosome aneuploidy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following discussion with a Clinical Geneticist to consider whether broader testing is more appropriate

Requesting Specialties

- Clinical Genetics
- Community Paediatrics
- Metabolic Medicine
- Neonatology
- Neurology
- Paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R28.1	Genomewide Microarray	Singleton	Genomewide CNVs	Genomewide	Genomewide	Microarray

R28先天畸形和畸形综合征-微阵列仅

检测标准

临床特征高度提示染色体病因，例如具有 Williams 综合征特征性表现的个体

在可能的情况下，应在检测申请单上注明所怀疑的染色体疾病。

R28 微阵列(基因芯片)检测并非在具有可能的单基因病因、且无特定染色体疾病(如 22q11 缺失综合征)可识别特征的综合征性儿科疾病患者中启动 R27 之前的要求。

重叠指征

- 在染色体病因可能性较低的情况下，应改用 R27 儿科疾病检测较低
- 当临床特征强烈提示时，应使用 R26 可能常见非整倍体检测13、18 或 21 三体，Turner 综合征或其他性染色体非整倍体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，经与临床遗传学家讨论以考虑更广泛的检测是否更为合适

申请专科

- 临床遗传学
- 社区儿科
- 代谢医学
- 新生儿科
- 神经科
- 儿科

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R28.1	全基因组范围微阵列（基因芯片）	单人	全基因组范围拷贝数变异	全基因组范围	全基因组范围	微阵列（基因芯片）

R47 Angelman syndrome

Testing Criteria

1. Molecular findings suggestive of Angelman syndrome from, for example microarray, exome or genome analysis such as likely isodisomy or deletion at 15q11-13; OR
2. Clinical features strongly suggestive of Angelman syndrome

Overlapping indications

- R27 Paediatric disorders or other relevant broader tests should be used in preference individuals where Angelman syndrome is plausible but not highly likely
- R263 Confirmation of uniparental disomy test should be used to confirm likely UPD detected on methylation and copy number testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following identification of likely assessment by a Consultant Clinical Geneticist or Paediatric Neurologist

Requesting Specialties

- Clinical Genetics
- Genomics laboratory
- Neurology
- Community paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R47.1	AS/PWS critical region Methylation testing	Singleton	Methylation, CNVs	Single interval	AS/PWS critical region	Methylation testing

R47Angelman综合征

检测标准

1. 来自例如微阵列(基因芯片)、外显子组或基因组分析的提示 Angelman 综合征的分子发现例如 15q11-13 的可能同源二体或缺失；或 2. 临床特征强烈提示Angelman 综合征

重叠指征

• 对于以下个体，应优先使用 R27 儿科疾病或其他相关更广泛的检测 Angelman 综合征有可能，但可能性不高

• 应使用 R263 单亲二体确认检测来确认在以下检测中发现的可能 UPD 甲基化与拷贝数检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在经临床遗传学顾问或儿科神经科医生评估发现可能的之后

申请专科

• 临床遗传学

• 基因组实验室

• 神经科

• 社区儿科

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R47.1	AS/PWS 关键区域甲基化检测	单人	甲基化，拷贝数变异	单一区间	AS/PWS关键区域	甲基化检测

R48 Prader-Willi syndrome

Testing Criteria

1. Molecular findings suggestive of Prader-Willi syndrome from, for example microarray, exome or genome analysis such as likely isodisomy or deletion at 15q11-13; **OR**
2. Clinical features strongly suggestive of Prader-Willi syndrome. All of the following should be present for a given age group:

   Neonatal period: Hypotonia with poor suck

   Age one month to two years:
   - Hypotonia with poor appetite and suck in the neonatal period
   - Developmental delay

   Age two to six years:
   - Hypotonia with history of poor suck
   - Developmental delay

   Age six to adulthood:
   - History of hypotonia with poor suck (hypotonia often persists)
   - Developmental delay
   - Excessive eating with central obesity if uncontrolled externally
   - Hypothalamic hypogonadism (when developmentally relevant)

Overlapping indications

- R27 Paediatric disorders, or other relevant broader tests should be used in preference for individuals where Prader-Willi syndrome is plausible but not highly likely.
- R263 Confirmation of uniparental disomy test should be used to confirm likely UPD detected on methylation and copy number testing.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Genomics laboratory
- Neonatology
- Community paediatrics
- Neurology
- Paediatrics
- Endocrinology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R48.1	AS/PWS critical region Methylation testing	Singleton	Methylation, CNVs	Single interval	AS/PWS critical region	Methylation testing

R48Prader-Willi综合征

检测标准

1. 来自例如微阵列(基因芯片)、外显子组或基因组分析的提示 Prader-Willi 综合征的分子发现，例如 15q11-13 的可能同源二体或缺失；**或**

2. 临床特征强烈提示 Prader-Willi 综合征。对于特定年龄组，以下各项均应存在：

   新生儿期：肌张力低下伴吸吮无力

   1月龄至2岁：
   - 新生儿期肌张力低下伴食欲差及吸吮无力
   - 发育迟缓

   两岁至六岁：
   - 肌张力低下伴吸吮无力史
   - 发育迟缓

   六岁至成年：
   - 肌张力低下伴吸吮无力的病史(肌张力低下常持续存在)
   - 发育迟缓
   - 外部控制不佳时出现过度进食伴中心性肥胖
   - 下丘脑性性腺功能减退症(当与发育相关时)

重叠指征

- 对于 Prader-Willi 综合征合理但非高度可能的个体，应优先使用 R27 儿科疾病或其他相关更广泛的检测。
- 应使用 R263 单亲二体确认检测来确认在甲基化和拷贝数检测中发现的可能 UPD。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 基因组实验室
- 新生儿科
- 社区儿科
- 神经科
- 儿科
- 内分泌学

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R48.1	AS/PWS 关键区域甲基化检测	单人	甲基化，拷贝数变异	单一区间	AS/PWS关键区	甲基化检测

R69 Hypotonic infant

Testing Criteria

Neonates or infants with unexplained hypotonia where the clinical picture is suggestive of a central cause, i.e. particularly where the baby is not alert, but lethargic or sleepy

Overlapping indications

- R70 Spinal muscular atrophy type 1 diagnostic test and/or R48 Prader Willi syndrome and/or R72 Myotonic dystrophy and/or R452 Silver Russel Syndrome /Temple Syndrome or other tests for neuromuscular causes should be used where the baby is alert and responsive and the floppiness appears static over a period of days.
- **R14 Acutely unwell children with a likely monogenic disorder, should be used for acutely unwell neonates with hypotonia. Please note that myotonic dystrophy, SMA, Prader Willi syndrome and Silver Russel Syndrome / Temple syndrome are not tested for within R14 and need to be requested separately.**

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation after exclusion of sepsis or hypoglycaemia as causes

Requesting Specialties

- Clinical Genetics
- Community Paediatrics
- Neonatology
- Neurology
- Paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R69.5	Hypotonic infant W	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Hypotonic infant (490)	WGS

R69肌张力低下婴儿

检测标准

患有不明显原因肌张力低下的新生儿或婴儿，其临床表现提示中枢性病因，即特别是婴儿不警觉，而是昏睡或嗜睡

重叠指征

- R70 脊髓性肌萎缩症 1 型诊断检测和/或 R48 Prader Willi 综合征和/或 R72
  当婴儿警觉且有反应，且松软状态在数日内似乎静止时，应使用强直性肌营养不良和/或 R452 Silver Russel 综合征/Temple 综合征或其他神经肌肉病因检测。
- **对于伴有肌张力低下的急性不适新生儿，应使用 R14 可能为单基因疾病的急性不适儿童检测。请注意，强直性肌营养不良、SMA、Prader Willi 综合征和 Silver Russel 综合征/Temple 综合征不在 R14 内检测，需单独申请。**

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在排除脓毒症或低血糖作为病因后

申请专科

- 临床遗传学
- 社区儿科
- 新生儿科
- 神经科
- 儿科

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R69.5	肌张力低下婴儿 W Trio 或单例外显子水平		CNV，小变异、STRs	基因检测板或基因座	肌张力低下婴儿 (490)	全基因组测序

R312 Parental sequencing for lethal autosomal recessive disorders

Testing Criteria

1. Lethal disorder with likely autosomal recessive inheritance in which there is limited or no DNA from the deceased individual, AND
2. Both parents are available for testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

As appropriate

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Other

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R312.1	Relevant panels in PanelApp or gene agnostic WES or large panel	Parents only	Small variants, CNVs	Panel of genes or loci	Relevant panel(s) in PanelApp	WES or large panel

R312致死性常染色体隐性疾病的父母测序

检测标准

1. 可能为常染色体隐性遗传的致死性疾病，其中来自以下来源的 DNA 有限或没有已故个体，且
2. 父母双方均可进行检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

酌情

申请专科

• 临床遗传学

专科服务组

• 其他

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R312.1	相关检测组合位于PanelApp或基因未知WES或大检测	仅父母	小变异，拷贝数变异	基因检测板或基因座	PanelApp中的相关检测组合	WES或大检测组合

Part IV. Endocrinology

R402 Premature ovarian insufficiency

Testing Criteria

1. Four consecutive months of unexplained amenorrhoea (primary or secondary), AND
2. Elevated serum FSH of >30IU/L on two separate occasions at least 6 weeks apart, AND
3. Age of onset is <30 years, AND
4. Non-genetic causes have been excluded including presence of thyroid and adrenal auto-antibodies

To note: Application of either karyotype or Targeted Chromosome Analysis (TCA) will be directed by professional judgement, best practice recommendation, clinical context and/or the type of cytogenetic rearrangement(s) detected. Due to the nature of cytogenetic analysis, reportable cytogenetic incidental findings may be detected during TCA.

Overlapping indications

- R54 Hereditary ataxia with onset in adulthood test should be used in preference in individuals with adult onset ataxia given the broad range of possible causes

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

N/A

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Gynaecology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R402.1	Premature ovarian insufficiency .	Singleton	Structural variants	Genomewide	Genomewide	Karyotype / TCA
R402.2	FMR1 STR testing	Singleton	STRs	Single interval	FMR1 STR	STR testing

第四部分IV.内分泌学

R402早发性卵巢功能不全

检测标准

1. 连续四个月不明原因的闭经(原发性或继发性)，且
2. 两次独立检测(间隔至少6周)血清FSH升高>30IU/L，且
3. 发病年龄<30岁,且
4. 已排除非遗传性病因，包括存在甲状腺和肾上腺自身抗体

注意：采用核型分析或靶向染色体分析(TCA)将由专业判断、最佳实践建议、临床背景和/或所检测到的细胞遗传学重排类型决定。由于细胞遗传学分析的性质，在TCA过程中可能检测到可报告的细胞遗传学偶然发现。

重叠指征

• 对于成人起病者，应优先使用R54成人起病遗传性共济失调检测
鉴于可能病因范围广泛，共济失调的起病

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 内分泌学
• 妇科

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R402.1	卵巢早衰功能不全。	单人	结构变异	全基因组范围	全基因组范围	核型分析 / TCA
R402.2	FMR1短串联重复序列检	单人	短串联重复序列	单一区间	FMR1 短串联重复序列	短串联重复序列检测

R314 Ambiguous genitalia

Testing Criteria

Presentation of ambiguous genitalia to test for sex chromosome aneuploidy, mosaicism, and/or structural rearrangement. For neonates, rapid testing may be necessary for management purposes.

To note: Application of either karyotype or Targeted Chromosome Analysis (TCA) will be directed by professional judgement, best practice recommendation, clinical context and/or the type of cytogenetic rearrangement(s) detected. Due to the nature of cytogenetic analysis, reportable cytogenetic incidental findings may be detected during TCA.

Overlapping indications

- R180 Congenital adrenal hyperplasia diagnostic test may be required if aneuploidy test and biochemical investigations suggest this is the likely diagnosis
- R146 Differences in sex development test may be required if underlying diagnosis still unclear after aneuploidy test, CAH test (where relevant) and biochemical investigations

Where in Pathway

Urgently at presentation, in parallel with biochemical investigations for potential salt-losing crisis where CAH is the likely diagnosis

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Neonatology

Specialist Service Group

- Core

Associated Tests

Please note that not all the associated tests below will be undertaken in every case. The reason for referral or initial results will indicate which tests are required.

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R314.1	Ambiguous genitalia	Singleton	Aneuploidy	Genomewide	Sex chromosomes	Common aneuploidy testing
R314.2	Ambiguous genitalia	Singleton	Chromosome imbalance and/or structural variants	Genomewide	Sex chromosomes	Karyotype / Targeted Chromosome Analysis

R314生殖器性别不明

检测标准

外生殖器模糊者，检测性染色体非整倍体、嵌合现象和/或结构重排。对于新生儿，为便于管理可能需要快速检测。

注意：采用核型分析或靶向染色体分析(TCA)将由专业判断、最佳实践建议、临床背景和/或所检测到的细胞遗传学重排类型决定。由于细胞遗传学分析的性质，在TCA过程中可能检测到可报告的细胞遗传学偶然发现。

重叠指征

- 如果非整倍体检测和生化检测[结果不明确]，可能需要R180先天性肾上腺增生诊断检测检查提示这可能是最可能的诊断
- 如果在[初步评估]后基础诊断仍不明确，可能需要R146性发育差异检测非整倍体检测、CAH 检测(如相关)及生化检查

通路中的位置

就诊时紧急进行，与生化检查同步进行，以应对CAH为可能诊断时潜在的失盐危象

申请专科

- 临床遗传学
- 内分泌学
- 新生儿科

专科服务组

- 核心

相关检测

请注意，并非每个病例都会进行以下所有相关检测。转诊原因或初始结果将指示需要哪些检测。

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R314.1	模糊生殖器	单人	非整倍体	全基因组范围	性染色体	常见非整倍体检测
R314.2	模糊生殖器	单人	染色体失衡和/或结构变异	全基因组范围	性染色体	核型分析 / 靶向染色体分析

R106 Alstrom syndrome

Testing Criteria

Clinical features strongly indicative of a diagnosis of Alstrom syndrome including at least two of the following:

1. Hepatobiliary disease
2. Retinal degeneration
3. Childhood onset obesity
4. Renal disease

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals overlapping or atypical presentations where features are not characteristic of Alstrom syndrome specifically

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics
- Endocrinology
- Ophthalmology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R106.1	ALMS1 Single gene sequencing	Singleton	Small variants	Single gene(s)	ALMS1 (1210)	Single gene sequencing >=10 amplicons

R106Alstrom综合征

检测标准

临床特征强烈提示Alstrom综合征诊断，包括以下至少两项：1. 肝胆疾病

2. 视网膜变性
3. 儿童期起病肥胖
4. 肾脏疾病

重叠指征

• 对于表现重叠或非典型、特征不符合Alstrom的个体，应使用R27儿科疾病或R89超罕见和非典型单基因疾病检测

综合征具体而言

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 心脏病学
• 临床遗传学
• 内分泌学
• 眼科

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R106.1	ALMS1单基因测序	单人	小变异	单基因	ALMS1 (1210)	单基因测序 >=10扩增子

R141 Monogenic diabetes

Testing Criteria

1. **Patients with isolated diabetes** should be tested if they have:

a. **Diabetes diagnosed young** (≤35 years in White Europeans and ≤30 years in high prevalence ethnic groups).

AND

b. **Unlikely to have Type 1 diabetes** because:
They are not on insulin treatment.
OR
They are on insulin treatment with all autoantibodies tested negative (minimum testing of GADA and IA2A) and a random non-fasting C peptide value ≥200pmol/l

AND

c. **Have features suggestive of MODY:**
An HbA1c at diagnosis of diabetes <7.5% (58mmol/mol), if diagnosed under 18 years of age,
OR
BMI <30kg/m^2 adult (child BMI <95th centile) **and** a parent with diabetes (if White) or BMI <27kg/m^2 (child BMI <95th centile) **and** a parent with diabetes (if high prevalence type 2 diabetes ethnic group).
OR
Have a MODY probability score ≥20% if not insulin treated and ≥10% if insulin treated (see https://www.diabetesgenes.org/exeter-diabetes-app/ModyCalculator)

2. **Syndromic diabetes:** Patients with diabetes **AND** non-autoimmune extra-pancreatic features

- Diabetes diagnosed young

AND

- Unlikely to have type 1 diabetes (see 1b) or type 2 diabetes.

AND

- Non-autoimmune extra pancreatic features suggestive of syndromic monogenic diabetes
e.g.
    - Cystic renal disease and/or congenital anomaly of kidney or urinary tract
    - Bilateral sensorineural deafness
    - Developmental delay
    - Developmental defects
    - Cardiomyopathy
    - Optic atrophy
    - Microcephaly

3. **Diabetes with severe insulin resistance**

- Patients have features of severe insulin resistance in the absence of obesity:
    - Acanthosis nigricans
    OR
    - A fasting insulin ≥150pmol/l if not insulin treated **OR** if insulin treated an insulin requirement >3U/kg/day

AND

- Diabetes that is unlikely to be type 1 diabetes (see 1.0 above) or type 2 diabetes (BMI<30kg/m^2 if white (<95th in children) or BMI <27kg/m^2 (<95th in children) if high prevalence type 2 diabetes group).

Overlapping indications

- R158 Severe insulin resistance and lipodystrophy syndromes, test should be used for congenital severe syndromic forms of lipodystrophy.
- R142 Glucokinase-related fasting hyperglycaemia test should be used for asymptomatic fasting hyperglycaemia.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation; HbA1C testing is required prior to genetic testing

R141单基因糖尿病

检测标准

1. **孤立性糖尿病患者**若符合以下情况应进行检测：

a.**年轻时诊断糖尿病**(白人欧洲人≤35岁，高患病率族群≤30岁)。

和

b. **不太可能为1型糖尿病**，因为：未接受胰岛素治疗。**或**正在接受胰岛素治疗，所有检测的自身抗体均为阴性(至少检测GADA和IA2A)，且随机非空腹C肽值≥200pmol/l

和

c. **具有提示MODY的特征：**诊断糖尿病时HbA1c <7.5%(58mmol/mol),若诊断年龄在18岁以下,**或**成人BMI <30kg/m^2(儿童BMI <95th百分位)**且**父母一方患糖尿病(若为白人)或BMI <27kg/m^2(儿童BMI <95th百分位)**且**父母一方患糖尿病(若为2型糖尿病高患病率族群)。**或**MODY概率评分≥20%(若未接受胰岛素治疗)且≥10%(若接受胰岛素治疗)(见https://www.diabetesgenes.org/exeter-diabetes-app/ModyCalculator)

2. **综合征性糖尿病：**患有糖尿病**且**具有非自身免疫性胰腺外特征的患者

• 年轻时诊断的糖尿病

和

• 不太可能患有1型糖尿病(见1b)或2型糖尿病。

和

• 提示综合征性单基因糖尿病的非自身免疫性胰腺外特征
例如
    • 囊性肾病和/或肾脏或泌尿道先天性异常
    • 双侧感音神经性耳聋
    • 发育迟缓
    • 发育缺陷
    • 心肌病
    • 视神经萎缩
    • 小头畸形

3. **伴严重胰岛素抵抗的糖尿病**

• 患者在没有肥胖的情况下表现出严重胰岛素抵抗的特征：
    • 黑棘皮病
    或
    • 未接受胰岛素治疗时空腹胰岛素>150pmol/l **或**接受胰岛素治疗时胰岛素需求量>3U/kg/天

和

• 不太可能为1型糖尿病(见上文1.0)或2型糖尿病(白人BMI<30kg/m ^{2}(儿童<第95百分位)或高患病率2型糖尿病族群BMI<27kg/m ^{2}(儿童<第95百分位))的糖尿病。

重叠指征

• R158严重胰岛素抵抗和脂肪营养不良综合征，应用于先天性严重综合征性脂肪营养不良类型。

• R142葡萄糖激酶相关空腹高血糖检测应用于无症状空腹高血糖。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时；基因检测前需进行HbA1C检测

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Nephrology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R141.1	Monogenic diabetes WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Monogenic diabetes (472)	WES or Medium Panel

申请专科

- 临床遗传学
- 内分泌学
- 肾脏科

专科服务组

- 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R141.1	单基因糖尿病 WES 或中通量面板	单人	小变异，拷贝数变异	基因检测板或基因座	单基因糖尿病 (472)	WES或Medium检测板

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R142 Glucokinase-related fasting hyperglycaemia

Testing Criteria

Fasting glucose noted to be raised ≤35 years

AND

Asymptomatic stable fasting hyperglycaemia (5.5-8mmol/L) (minimum 2 independent laboratory fasting blood glucose test results)

OR

HbA1c 36-58mmol/mol (5.5-7.5%)

In pregnancy

a) Gestational diabetes with fasting glucose 5.5-8mmol/l.

AND

b) BMI <30kg/m^2 if white, or BMI <27kg/m^2, if high prevalence type 2 diabetes ethnic group.

Features that support a diagnosis in pregnancy: persistent fasting hyperglycaemia post pregnancy or previous babies with normal birthweight despite maternal hyperglycaemia.

HbA1c and fasting glucose results must be available prior to genetic testing.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

HbA1C and fasting glucose results must be available prior to genetic testing

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Specialist midwifery

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R142.1	GCK Single gene sequencing	Singleton	Small variants	Single gene(s)	GCK (1338)	Single gene sequencing >=10 amplicons

R142葡萄糖激酶相关空腹高血糖

检测标准

空腹血糖升高，记录于≤35岁

和

无症状稳定性空腹高血糖(5.5-8mmol/L)(至少2次独立实验室空腹血糖检测结果)

或

HbA1c 36-58mmol/mol（5.5-7.5%）

妊娠期

a) 妊娠期糖尿病，空腹血糖5.5-8mmol/l。

和

b) 白人BMI<30kg/m ^{2}，或高患病率2型糖尿病族群BMI<27kg/m ^{2}。

支持妊娠期诊断的特征：妊娠后持续性空腹高血糖，或既往婴儿出生体重正常但母亲存在高血糖。

HbA1c 和空腹血糖结果必须在基因检测前获得。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

基因检测前必须可获得HbA1C和空腹血糖结果申请专科

• 临床遗传学

• 内分泌学

• 专科助产

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R142.1	GCK单基因测序	单人	小变异	单基因	GCK (1338)	单基因测序 >=10扩增子

R143 Neonatal diabetes

Testing Criteria

All patients diagnosed with diabetes diagnosed less than 9 months of age.

Marked hyperglycaemia is common in very preterm patients due to an immature pancreas. These individuals should be referred for genetic testing only if hyperglycaemia requiring insulin treatment is still present at 32 weeks equivalent gestational age.

Where possible, clinicians are asked to submit samples from the probands parents for the DNA to be stored (R346) to allow follow-up of variants

Order of testing

Start with treatment response screen for sulphonylurea-sensitive genes by using R143.1

Continue to panel test if negative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Genomics laboratory
- Neonatology

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R143 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R143.1	ABCC8; KCNJ11	Singleton	Small variants	Small panel	ABCC8; KCNJ11 (1369)	Small panel
R143.3	6q24 Methylation testing	Singleton	Methylation	Single interval	6q24	Methylation testing
R143.4	Diabetes - neonatal onset WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Diabetes - neonatal onset (293)	WGS

R143新生儿糖尿病

检测标准

所有诊断为糖尿病且诊断年龄小于9个月的患者。

明显的高血糖在极早产儿中常见，原因是胰腺发育不成熟。只有当校正胎龄32周时仍需胰岛素治疗的高血糖持续存在时，这些个体才应转诊进行基因检测。

在可能的情况下，请临床医生提交先证者父母的样本用于DNA储存(R346)，以便对变异进行随访

检测顺序

首先使用R143.1进行磺脲类药物敏感基因的治疗反应筛查。若为阴性，继续进行panel检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 内分泌学
- 基因组实验室
- 新生儿科

专科服务组

- 内分泌学

相关检测

请注意，对于R143临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均无必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R143.1	ABCC8; KCNJ11	单人	小变异	小检测板	ABCC8; KCNJ11 (1369)	小检测板
R143.3	6q24甲基化检测	单人	甲基化	单一区间	6q24	甲基化检测
R143.4	糖尿病 - 新生儿发病 WGS（阶段 1）	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	糖尿病 - 新生儿期发病 (293)	全基因组测序

R145 Congenital hypothyroidism

Testing Criteria

1. Congenital hypothyroidism, thyroid hypoplasia or agenesis with or without syndromic features, OR
2. Thyroid dyshormonogenesis, OR
3. Raised serum thyroid stimulating hormone (TSH) level:
   a. With enlarged thyroid gland, OR
   b. In the absence of thyroid autoantibodies

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R145.1	Congenital hypothyroidism WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Congenital hypothyroidism (31)	WES or Medium panel

R145先天性甲状腺功能减退症

检测标准

1. 先天性甲状腺功能减退症、甲状腺发育不全或甲状腺缺如，伴或不伴综合征特征，或
2. 甲状腺激素合成障碍，OR
3. 血清促甲状腺激素(TSH)水平升高：
   a. 伴甲状腺肿大，或
   b. 在缺乏甲状腺自身抗体的情况下

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R145.1	先天性甲状腺功能减退症 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	先天性甲状腺功能减退症 (31)	WES或Medium检测组合

R329 Familial dysalbuminaemic hyperthyroxinaemia

Testing Criteria

Raised serum T4 with inappropriately non-suppressed serum TSH

[Attempt to exclude assay interference as a cause of the abnormal TFT result prior to genetic test]

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R329.1	ALB Single gene sequencing	Singleton	Small variants	Single gene(s)	ALB (1333)	Single gene sequencing >=10 amplicons

R329家族性白蛋白异常性高甲状腺素血症

检测标准

血清T4升高伴血清TSH不适当未受抑制

[在基因检测前尝试排除检测干扰作为甲状腺功能检查结果异常的原因]

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R329.1	ALB单基因测序	单人	小变异	单基因	ALB (1333)	单基因测序 >=10扩增子

R182 Hyperthyroidism

Testing Criteria

Hyperthyroidism where common causes have been excluded:

1. Clinical exclusion of common causes such as toxic solitary nodules or multinodular goitre, AND
2. Graves disease excluded by negative TSH receptor autoantibodies when the patient is biochemically hyperthyroid, AND
3. Patient presenting below the age of 18 OR patient has a first degree relative with unexplained hyperthyroidism

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R182.1	Hyperthyroidism Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Hyperthyroidism (236)	Small panel

R182甲状腺功能亢进症

检测标准

甲状腺功能亢进症，已排除常见病因：

1. 临床排除常见原因，如毒性孤立性结节或多结节性甲状腺肿，且
2. 患者生化检查为甲状腺功能亢进时，TSH受体自身抗体阴性排除Graves病，且

3. 患者就诊年龄小于18岁，或患者有一级亲属患有不明原因的
甲状腺功能亢进症

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R182.1	甲状腺功能亢进症小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	甲状腺功能亢进症 (236)	小检测板

R146 Differences in sex development

Testing Criteria

XX or XY chromosomal sex is confirmed AND one of:

1. Ambiguous genitalia
2. Evidence of gonadal dysgenesis
3. Clinical symptoms of adrenal hypoplasia
4. Under virilisation in an individual assigned male at birth
5. Virilisation in an individual assigned female at birth
6. Urine steroid profile suggestive of DSD
7. Pubertal failure
8. Precocious puberty
9. Primary amenorrhea
10. Very early onset hypertension with evidence of pubertal or electrolyte disturbance

NOTE: Panel testing may be appropriate in patients with abnormal sex chromosome karyotypes, if on expert review the karyotype result is not thought to explain the DSD phenotype

NOTE: The common Congenital Adrenal Hyperplasia (CAH) gene CYP21A2 is too complex to examine using a next generation sequencing test under this indication. If a diagnosis of CAH due to 21-hydroxylase deficiency is suspected please request additional testing (see overlapping indications)

Overlapping indications

- R314 Ambiguous genitalia, should be used to establish karyotypic sex in urgent neonatal situations
- R180 Congenital adrenal hyperplasia diagnostic test should be used before the panel test where CAH is the likely diagnosis; the common CAH gene CYP21A2 is too complex to examine using a next generation sequencing test under this indication
- R468 Possible sex chromosome aneuploidy or structural rearrangement – Targeted Chromosome Analysis

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

After urgent neonatal testing is complete where indicated, in the absence of a diagnosis; at presentation for non-neonatal situations

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Gynaecology

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R146 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R146.1	Genomewide Microarray	Singleton	Genomewide CNVs	Genomewide	Genomewide	Microarray
R146.2	Differences in sex development WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Differences in sex development (9)	WES or Medium Panel

R146性发育差异检测标准

XX 或 XY 染色体性别已确认，且符合以下任一条件：

1. 外生殖器性别不清
2. 性腺发育不全的证据
3. 肾上腺发育不全的临床症状
4. 在出生时被指定为男性的个体中，在男性化表现下
5. 出生时被指定为女性的个体出现男性化
6. 尿液类固醇谱提示DSD
7. 青春期发育失败
8. 性早熟
9. 原发性闭经
10. 极早发高血压，伴有青春期或电解质紊乱的证据

注：对于性染色体核型分析异常的患者，如果经专家审查认为核型分析结果不能解释DSD表型，panel检测可能是合适的

注：常见的先天性肾上腺增生症(CAH)基因CYP21A2过于复杂，无法在该指征下使用下一代测序检测进行检查。如果怀疑因21-羟化酶缺乏症导致的CAH诊断，请申请额外检测(参见重叠指征)

重叠指征

• R314 外生殖器模糊，应用于紧急新生儿情况下确定核型性别

• R180 先天性肾上腺增生症诊断检测应在CAH为可能诊断时于panel检测之前使用；常见的CAH基因CYP21A2过于复杂，无法在该指征下使用下一代测序检测进行检查

• R468 可能的性染色体非整倍体或结构重排 - 靶向染色体分析

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在指征明确的情况下完成紧急新生儿检测后，若无诊断；在非新生儿情况下就诊时

申请专科

• 临床遗传学

• 内分泌学

• 妇科

专科服务组

• 内分泌学

相关检测

请注意，对于R146临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均无必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R146.1	全基因组范围微阵列（基因芯片）	单人	全基因组范围拷贝数变异	全基因组范围	全基因组范围	微阵列（基因芯片）
R146.2	性别差异发育 WES或中等 panel	单人	小变异，拷贝数变异	基因检测板或基因座	性发育差异(9)	WES或Medium检测板

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R452 Silver Russell Syndrome and Temple Syndrome

Testing Criteria

Clinical features strongly indicative of a diagnosis of Silver-Russell syndrome, as assessed by the presence of 3 or more of the features below*:

1. Small Gestational Age (birth weight and/or birth length): ≤−2 standard deviation score (SDS) for gestational age
2. Postnatal growth failure: Height at 24 ± 1 months ≤−2 SDS or height ≤−2 SDS below mid-parental target height
3. Relative macrocephaly at birth: Head circumference at birth ≥1.5 SDS above birth weight and/or length
4. Protruding forehead: Forehead projecting beyond the facial plane on a side view as a toddler (1–3 years)
5. Body asymmetry: Leg length discrepancy of ≥0.5 cm or arm asymmetry or leg length discrepancy <0.5 cm with at least two other asymmetrical body parts (one non-face)
6. Feeding difficulties and/or low BMI: BMI ≤−2 standard deviations at 24 months or current use of a feeding tube or cyproheptadine for appetite stimulation

*See Wakeling et al 2017, PMID: 27585961

OR

Clinical features suggestive or Temple Syndrome for the relevant age group:

Infant and young child (age 1 – 3 years), **three or more** of the following:

- SGA (small for gestational age) or IUGR (intrauterine growth restriction)
- Postnatal growth failure
- Hypotonia at birth
- Feeding difficulties
- Relative macrocephaly at birth
- Motor and/or speech delay

Child (age 4 – 10 years), **three or more** of the following:

- SGA or IUGR
- Postnatal growth failure
- Hypotonia at birth
- Feeding difficulties in infancy
- Relative macrocephaly at birth
- Motor and/or speech delay
- Precocious puberty
- Learning difficulties
- Increased BMI

Teen (11 – 18 years) and adult (>18 years), **four or more** of the following:

- SGA or IUGR
- Postnatal growth failure
- Hypotonia at birth
- Feeding difficulties in infancy
- Relative macrocephaly at birth
- Motor and/or speech delay
- Precocious puberty
- Learning difficulties
- Increased BMI

R452SilverRussell综合征和Temple综合征

检测标准

临床特征强烈提示Silver-Russell综合征诊断，经评估存在以下3项或以上特征*:

1. 小于胎龄(出生体重和/或出生身长)：按胎龄计≤–2个标准差评分(SDS)
2. 出生后生长障碍：24 ± 1 月龄时身高 ≤–2 SDS，或身高低于中亲靶身高 ≤–2 SDS
3. 出生时相对大头畸形：出生时头围≥1.5 SDS高于出生体重和/或身长
4. 前额突出：幼儿期(1-3岁)侧视时前额突出于面部平面
5. 身体不对称：腿长差异≥0.5 cm或手臂不对称或腿长差异<0.5 cm且至少有两个其他不对称身体部位(一个非面部)
6. 喂养困难和/或低BMI:24月龄时BMI≤–2个标准差或当前使用喂养管或赛庚啶刺激食欲 *参见Wakeling等2017,PMID:27585961

或

提示相关年龄组Temple综合征的临床特征：婴幼儿(1 - 3岁)，符合以下三项或以上：

- 小于胎龄儿(SGA)或宫内生长受限(IUGR)
- 出生后生长障碍
- 出生时肌张力低下
- 喂养困难
- 出生时相对大头畸形
- 运动及/或言语发育迟缓

儿童(4 - 10岁)，以下情况中**三项或以上**:

- SGA或IUGR
- 出生后生长障碍
- 出生时肌张力低下
- 婴儿期喂养困难
- 出生时相对大头畸形
- 运动及/或言语发育迟缓
- 性早熟
- 学习困难
- BMI升高

青少年(11 - 18岁)和成人(>18岁),**四项或以上**以下表现：

- SGA或IUGR
- 出生后生长障碍
- 出生时肌张力低下
- 婴儿期喂养困难
- 出生时相对大头畸形
- 运动及/或言语发育迟缓
- 性早熟
- 学习困难
- BMI升高

Overlapping indications

- R88 Severe microcephaly test should be used for patients with primary microcephaly – microcephalic dwarfism spectrum.
- R159 Pituitary hormone deficiency test should be used where more than one pituitary hormone is deficient as the cause of growth failure
- R104 Skeletal dysplasia should be considered if overlapping features are present and should be used where clinical features indicative of a likely monogenic skeletal dysplasia
- R52 Short stature – SHOX deficiency – where clinical features are strongly indicative of SHOX deficiency
- R453 Monogenic short stature – if the primary clinical presentation is short stature and not skeletal dysplasia or a more complex paediatric syndromic disorder
- R27 Paediatric Disorders if the presentation appears syndromic
- R26 Likely common aneuploidy for suspected Turner Syndrome

Where in Pathway

At presentation,.

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Paediatrics

Specialist Service Group

- Endocrinology

Associated Tests

Please note: the methylation-sensitive MLPA assay commonly used for this clinical indication includes probes for the chromosome 7 and chromosome 11 loci associated with Silver-Russell syndrome as well as loci on chromosome 14 associated with Temple syndrome.

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R452.1	Silver Russell Syndrome and Temple Syndrome	Singleton	CNVs and methylation status	Single interval	11p15 imprinted growth regulatory region and UPD7 and UPD14 growth regulatory critical regions	Methylation testing

重叠指征

- R88 重度小头畸形检测应用于原发性小头畸形患者 - 小头畸形侏儒症谱系。
- R159 垂体激素缺乏检测应在一种以上垂体激素缺陷是生长失败的原因
- R104 骨骼发育不良应考虑在存在重叠特征时使用，并应用于临床特征提示可能为单基因骨骼发育不良
- R52 矮身材 - SHOX缺乏 - 临床特征强烈提示SHOX缺乏
- R453 单基因矮身材 - 如果主要临床表现是矮身材而非骨骼发育不良或更复杂的儿科综合征性障碍
- 若临床表现呈综合征性，则为 R27 儿童期疾病
- R26 疑似特纳综合征的常见非整倍体可能性较大

通路中的位置

申请专科

- 临床遗传学
- 内分泌学
- 儿科

专科服务组

- 内分泌学

相关检测

请注意：常用于该临床指征的甲基化敏感MLPA检测包括与Silver-Russell综合征相关的7号和11号染色体位点探针，以及与Temple综合征相关的14号染色体位点探针。

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R452.1	西尔弗-拉塞尔综合征和Temple综合征	单人	CNVs和甲基化状态	单一区间	11p15印记生长调控区和 UPD7 和UPD14生长调控关键区域	甲基化检测

R453 Monogenic short stature

Testing Criteria

1. Height < -3 Standard Deviation Scores (SDS) below the mean at the age of at least 2 years,
   - in the absence of microcephaly AND
   - with a normal short stature screen* (but no requirement for normal dynamic growth hormone test)

OR

2. Height -2 to -3 SDS below the mean at the age of at least 2 years,
   - in the absence of microcephaly AND
   - with a normal short stature screen* (but no requirement for normal dynamic growth hormone test) AND
   - height 3 centiles below mid parental centile AND
   - following discussion at a specialist MDT that includes paediatric endocrinology and clinical genetics.

* Normal short screen as per primary investigations recommended in children referred to secondary or tertiary care with short stature in the British Society for Paediatric Endocrinology and Diabetes recommendations.

Investigation	To detect or exclude
Biochemical	
Full Blood Count (FBC)	Anaemia*
Renal function (creatinine and electrolytes)	Renal disorders
Liver function test	Liver disease
Erythrocyte sedimentation rate (ESR)	Infection / inflammatory disorders*
Calcium, Phosphate, (Ca / PO_4) Alkaline Phosphatase (ALP)	Renal / Ca / PO_4 disorders
Tissue transglutaminase (TTG)	Coeliac disease
Immunoglobulin A (IgA)	Coeliac disease
Insulin Like Growth Factor – 1 (IGF-1) †	Growth hormone deficiency
Free thyroxine (fT4), thyroid stimulation hormone (TSH)	Hypothyroidism
Karyotype (or if available Follicle Stimulating Hormone (FSH) if <2 or > 9 yr) **	Turner syndrome
Radiological	
Bone age‡	Assess growth delay
Skeletal X-rays (if disproportion is present)	Skeletal dysplasia

Panel of investigations proposed in international consensus statements from Oostdijk et al, Cohen et al and Grote et al. *To screen for coeliac disease/cystic fibrosis; †undernutrition and chronic illness cause low values and < 3 years of age difficult to interpret as normal range encompasses lower limit of assay, **only in females, ‡less reliable under 2 years of age; anatomical abnormalities may also be detected and suggestive of skeletal dysplasia.

R453单基因矮身材

检测标准

1. 身高低于均值 - 3个标准差评分(SDS)以下，年龄至少2岁，
   - 在没有小头畸形 AND 的情况下
   - 矮身材筛查正常*(但不要求生长激素激发试验正常)

或

2. 身高低于均值 2 至 3 个 SDS，年龄至少 2 岁，
   - 在没有小头畸形 AND 的情况下
   - 矮身材筛查正常*(但不要求生长激素激发试验正常)
     和
   - 身高低于父母中位身高百分位3个百分位，且
   - 经包括儿科内分泌学和临床遗传学的专科MDT讨论后。

* 正常矮身材筛查依据英国儿科内分泌和糖尿病学会推荐中转诊至二级或三级医疗的矮身材儿童初始检查建议。

检查	检测或排除
生化	
全血细胞计数（FBC）	贫血*
肾功能(肌酐和电解质)	肾脏疾病
肝功能检查	肝脏疾病
红细胞沉降率(ESR)	感染/炎症性疾病*
钙、磷酸盐(Ca / PO_4)碱性磷酸酶(ALP)	肾脏/钙/磷酸盐紊乱
组织型转谷氨酰胺酶(TTG)	乳糜泻
免疫球蛋白A（IgA）	乳糜泻
胰岛素样生长因子-1(IGF-1)†	生长激素缺乏症
游离甲状腺素(fT4)、促甲状腺激素(TSH)	甲状腺功能减退症
核型(或若可获得，促卵泡激素激素(FSH)若<2或>9岁)**	特纳综合征
影像学	
骨龄‡	评估生长迟缓
骨骼X线检查(如存在不成比例)	骨骼发育不良

Oostdijk等、Cohen等和Grote等国际共识声明中提出的检查组合。*用于筛查乳糜泻/囊性纤维化；†营养不良和慢性疾病导致低值，且< 3岁时难以解读,因正常范围涵盖检测下限,**仅限女性,‡2岁以下可靠性较低;也可能检测到解剖异常并提示骨骼发育不良。

Testing may occasionally be appropriate outside of the above criteria following clinical agreement at a specialist MDT that includes paediatric endocrinology and clinical genetics.

The reason for testing outside of this criteria must be discussed and agreed with the testing laboratory prior to sending samples and discussing with the patient/family.

Overlapping indications

- R452 Silver Russell Syndrome and Temple Syndrome
- R88 Severe microcephaly – if the presentation includes severe microcephaly
- R27 Paediatric disorders – if the presentation appears syndromic
- R52 Short stature – SHOX deficiency – where clinical features are strongly indicative of SHOX deficiency
- R104 Skeletal dysplasia – if there is disproportion or a skeletal survey suggestive of primary bone pathology (outside of the SHOX remit)
- R26 Likely common aneuploidy for suspected Turner Syndrome

Where in Pathway

At presentation.

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Paediatrics

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R453.1	Monogenic short stature	Singleton	Small variants, CNVs	Panel of genes or loci	Monogenic short stature (1471)	WES or Medium panel

在包括儿科内分泌学和临床遗传学的专科MDT临床同意后，偶尔可能适合在上述标准之外进行检测。

在送检样本和与患者/家属讨论之前，必须与检测实验室讨论并同意在该标准之外进行检测的原因。

重叠指征

- R452 银罗素综合征与坦普尔综合征
- R88 严重小头畸形--若临床表现包括严重小头畸形
- R27 儿科疾病--若表现呈综合征性
- R52 矮身材 - SHOX缺乏 - 临床特征强烈提示SHOX缺乏
- R104 骨骼发育不良 - 如果存在不成比例或骨骼检查提示原发性骨病理学(SHOX 职责范围之外)
- R26 疑似特纳综合征的常见非整倍体可能性

通路中的位置

就诊时。

申请专科

• 临床遗传学

• 内分泌学

• 儿科

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R453.1	单基因矮小身材	单人	小变异，拷贝数变异	基因检测板或基因座	单基因矮小症（1471）	WES或Medium检测组合

R49 Beckwith-Wiedemann syndrome

Testing Criteria

Clinical features suggestive of Beckwith-Wiedemann syndrome defined as:

1. One or more cardinal feature, OR
2. Two or more suggestive features

Cardinal features

- Macroglossia*
- Exomphalos
- Lateralized overgrowth*
- Multifocal and/or bilateral Wilms tumour or nephroblastomatosis
- Hyperinsulinism (lasting >1 week and requiring escalated treatment)
- Pathology findings: adrenal cortex cytomegaly, placental mesenchymal dysplasia or pancreatic adenomatosis

Suggestive features:

- Birthweight >2 SDS above the mean
- Facial naevus simplex
- Polyhydramnios and/or placentomegaly
- Ear creases and/or pits
- Transient hypoglycaemia (lasting <1 week)
- Typical Beckwith–Wiedemann spectrum tumours (neuroblastoma, rhabdomyosarcoma, unilateral Wilms tumour, hepatoblastoma, adrenocortical carcinoma or phaeochromocytoma)
- Nephromegaly and/or hepatomegaly
- Umbilical hernia and/or diastasis recti

*See Brioude et al 2018, PMID: 29377879

Overlapping indications

- R27 Paediatric disorders test should be used for overgrowth syndromes where Beckwith-Wiedemann syndrome is unlikely
- R50 Isolated hemihypertrophy or macroglossia test should be used where those features are present in isolation
- R263 Confirmation of uniparental disomy test should be used to confirm likely UPD detected on methylation and copy number testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, in parallel with renal ultrasound scan to look for Wilms tumour or Wilms precursor lesions and referral for Clinical Genetics consultation.

Requesting Specialties

- Cancer
- Clinical Genetics
- Endocrinology
- Neonatology
- Paediatrics

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R49 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

R49Beckwith-Wiedemann综合征检测标准

贝克威思-威德曼综合征的临床特征定义为：

1. 一项或多项主要特征，或
2. 两个或更多提示性特征

主要特征

- 巨舌症*
- 脐膨出
- 偏侧过度生长*
- 多灶性和/或双侧 Wilms 瘤或肾母细胞瘤病
- 高胰岛素血症(持续 >1 周且需要升级治疗)
- 病理发现：肾上腺皮质巨细胞、胎盘间充质发育不良或胰腺腺瘤病

提示性特征：

- 出生体重高于平均值 >2 SDS
- 面部单纯性痣
- 羊水过多和/或胎盘增大
- 耳褶和/或耳凹
- 短暂性低血糖(持续<1周)
- 典型Beckwith-Wiedemann谱系肿瘤(神经母细胞瘤、横纹肌肉瘤、单侧Wilms肿瘤、肝母细胞瘤、肾上腺皮质癌或嗜铬细胞瘤)
- 肾肿大和/或肝肿大
- 脐疝和/或腹直肌分离 *见Brioude等2018,PMID: 29377879

重叠指征

- R27 儿科疾病检测应用于Beckwith-Wiedemann过度生长综合征综合征的可能性不大
- R50 孤立性偏侧肥大或巨舌症检测应在这些特征孤立存在时使用孤立存在
- R263 单亲二体确认检测应用于确认甲基化和拷贝数检测中发现的可能UPD

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，与肾脏超声扫描同步进行以寻找Wilms肿瘤或Wilms前驱病变，并转诊进行临床遗传学咨询。

申请专科

- 癌症
- 临床遗传学
- 内分泌学
- 新生儿科
- 儿科

专科服务组

- 内分泌学

相关检测

请注意，以下所有检测均将针对 R49 临床指征申请进行，除非临床表现和/或初步结果表明所有检测均无必要

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R49.1	11p15 imprinted growth regulatory region Methylation testing	Singleton	Methylation, CNVs	Single interval	11p15 imprinted growth regulatory region	Methylation testing
R49.3	CDKN1C Single gene sequencing	Singleton	Small variants	Single gene(s)	CDKN1C (1309)	Single gene sequencing >=10 amplicons

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R49.1	11p15印记生长调控区域甲基化检测	单人	甲基化，拷贝数变异	单一区间	11p15印记生长调控区域	甲基化检测
R49.3	CDKN1C单基因测序	单人	小变异	单基因	CDKN1C（1309）	单基因测序 >=10扩增子

R50 Isolated hemihypertrophy or macroglossia

Testing Criteria

Isolated hemihypertrophy, OR

Isolated macroglossia

Overlapping indications

- R49 Beckwith-Wiedemann syndrome test should be used where additional features suggestive of Beckwith-Wiedemann syndrome are present
- R452 Silver Russell Syndrome and Temple Syndrome test should be used where additional features suggestive of Silver-Russell syndrome are present
- R26 Likely common aneuploidy test should be used where macroglossia occurs in the presence of features suggestive of Down syndrome
- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with complex or syndromic presentations not suggestive of Beckwith-Wiedemann syndrome, Silver-Russell syndrome or Down syndrome.
- R263 Confirmation of uniparental disomy test should be used to confirm likely UPD detected on methylation and copy number testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, in parallel with renal ultrasound scan to look for Wilms tumour or Wilms precursor lesions and referral for Clinical Genetics consultation

Requesting Specialties

- Clinical Genetics
- Paediatrics

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R50 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R50.1	11p15 imprinted growth regulatory region Methylation testing	Singleton	Methylation, CNVs	Single interval	11p15 imprinted growth regulatory region	Methylation testing

R50孤立性偏侧肥大或巨舌症

检测标准

孤立性偏侧肥大，OR

孤立性巨舌症

重叠指征

• 当存在提示Beckwith-Wiedemann综合征的额外特征时，应使用R49 Beckwith-Wiedemann综合征检测

• 当存在提示Silver-Russell综合征的额外特征时，应使用R452 Silver Russell综合征和Temple综合征检测

• 当巨舌症伴随提示Down综合征的特征出现时，应使用R26可能常见非整倍体检测

• 对于具有复杂或综合征性表现但不提示Beckwith-Wiedemann综合征、Silver-Russell综合征或Down综合征的个体，应使用R27儿科疾病或R89超罕见和非典型单基因疾病检测。

• R263 单亲二体确认检测应用于确认甲基化和拷贝数检测中发现的可能UPD

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，与肾脏超声扫描同步进行以寻找Wilms肿瘤或Wilms前驱病变，并转诊进行临床遗传学咨询

申请专科

• 临床遗传学

• 儿科

专科服务组

• 内分泌学

相关检测

请注意，所有以下检测将针对R50临床指征请求进行，除非临床表现和/或初步结果指示所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R50.1	11p15印记生长调控区域甲基化检测	单人	甲基化，拷贝数变异	单一区间	11p15印记生长调控区域	甲基化检测

R268 Kagami-Ogata syndrome – paternal uniparental disomy 14

Testing Criteria

1. Clinical features suggestive of Kagami-Ogata syndrome (paternal UPD14), OR
2. Molecular findings indicative of UPD 14 in which methylation analysis is required to differentiate paternal UPD 14 from maternal UPD 14

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R268.1	UPD14 critical region Methylation testing	Singleton	Methylation CNVs	Single interval	UPD14 critical region	Methylation testing

R268Kagami-Ogata综合征-父源性单亲二体14

检测标准

1. 提示Kagami-Ogata综合征(父源性UPD14)的临床特征，或
2. 指示UPD 14的分子发现，需要甲基化分析以区分父源性UPD 14与母源性UPD 14

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R268.1	UPD14关键区域甲基化检测	单人	甲基化 拷贝数变异	单一区间	UPD14关键区域	甲基化检测

R149 Severe early-onset obesity

Testing Criteria

BMI more than 3 standard deviations above the mean, with onset before the age of 5 years, in the absence of significant syndromic features, and with no explanation

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Paediatrics

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R149.1	Severe early-onset obesity WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Severe early-onset obesity (130)	WES or Medium panel

R149重度早发性肥胖

检测标准

BMI超过均值3个标准差以上，发病年龄在5岁之前，无显著综合征特征，且无其他解释

重叠指征

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 临床遗传学
• 内分泌学
• 儿科

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R149.1	严重早发性肥胖 WES 或中等 Panel	单人	小变异，拷贝数变异	基因检测板或基因座	重度早发性肥胖(130) WES或Medium	检测组合

R150 Congenital adrenal hypoplasia

Testing Criteria

Adrenal insufficiency as defined below, with no evidence of autoimmune Addisons disease, no biochemical evidence of congenital adrenal hyperplasia, and no other identifiable cause:

1. Combined primary glucocorticoid and mineralocorticoid insufficiency, OR
2. Isolated primary glucocorticoid insufficiency, OR
3. Isolated primary mineralocorticoid insufficiency

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R150.1	Congenital adrenal hypoplasia Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Congenital adrenal hypoplasia (145)	Small panel

R150先天性肾上腺发育不全

检测标准

如下定义的肾上腺功能不全，无自身免疫性Addison病证据，无先天性肾上腺增生的生化证据，且无其他可识别的原因：

1. 原发性糖皮质激素与盐皮质激素联合功能不全，或
2. 孤立性原发性糖皮质激素功能不全，OR
3. 孤立性原发性盐皮质激素功能不全

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R150.1	先天性肾上腺发育不全 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	先天性肾上腺发育不全 (145)	小检测板

R180 Congenital adrenal hyperplasia diagnostic test

Testing Criteria

Biochemically diagnosed Congenital Adrenal Hyperplasia (CAH) and at least one of the following:

1. Ambiguous genitalia or virilisation in an infant assigned female at birth, OR
2. Precocious puberty, OR
3. Accelerated pre-pubertal growth childhood with advanced bone age and evidence of adrenal steroid abnormality, OR
4. Salt-losing crisis in the neonatal period, OR
5. Infant electrolyte disturbance OR
6. Female adult with raised 17-OHP and at least one of the following: hirsutism, frontal baldness, delayed menarche or infertility

Overlapping indications

- R314 Ambiguous genitalia, test may be required before or in parallel to establish the diagnosis, particularly in the neonatal setting.
- R146 Differences in sex development test may be required after urgent neonatal testing if the diagnosis still isn't clear.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Neonatology
- Paediatrics

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R180 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R180.1	CYP21A2 Single gene sequencing	Singleton	Small variants	Single gene(s)	CYP21A2 (1317)	Single gene sequencing >=10 amplicons
R180.2	CYP21A2 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	CYP21A2 (1317)	MLPA or equivalent

R180先天性肾上腺增生诊断性检测检测标准

生化诊断为先天性肾上腺增生(CAH)且至少具备以下一项：

1. 出生时被指定为女性的婴儿出现外生殖器性别不清或男性化，或
2. 性早熟，OR
3. 儿童期青春期前生长加速伴骨龄提前及肾上腺类固醇异常证据，或
4. 新生儿期失盐危象，或
5. 婴儿电解质紊乱 OR
6. 成年女性17-OHP升高且至少具备以下一项：多毛症、额部秃发、月经初潮延迟或不孕

重叠指征

- R314 外生殖器模糊，可能需要在诊断建立之前或同时进行检测，尤其是在新生儿环境中。
- R146 性别发育差异检测可能需要在紧急新生儿检测后进行，如果诊断仍不明确。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 内分泌学
- 新生儿科
- 儿科

专科服务组

- 内分泌学

相关检测

请注意，以下所有检测将针对 R180 临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R180.1	CYP21A2单基因测序	单人	小变异	单基因	CYP21A2 (1317)	单基因测序 >=10扩增子
R180.2	CYP21A2 MLPA或等效	单人	外显子水平拷贝数变异	单基因	CYP21A2 (1317)	MLPA或等效

R181 Congenital adrenal hyperplasia carrier testing

Testing Criteria

Testing in partners of known carriers of CAH where management of a current or future pregnancy depends on the result

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At the time of reproductive planning

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R181 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R181.1	CYP21A2	Singleton	Small variants	Single gene(s)	CYP21A2	Single gene sequencing
R181.2	CYP21A2 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	CYP21A2	MLPA or equivalent

R181先天性肾上腺增生携带者检测

检测标准

对已知 CAH 携带者的伴侣进行检测，当前或未来妊娠的管理取决于检测结果

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在生育计划时

申请专科

• 临床遗传学

专科服务组

• 内分泌学

相关检测

请注意，对于 R181 临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R181.1	CYP21A2	单人	小变异	单基因	CYP21A2	单基因测序
R181.2	CYP21A2 MLPA或等效	单人	外显子水平拷贝数变异	单基因	CYP21A2	MLPA或等效

R183 Glucocorticoid-remediable aldosteronism (GRA)

Testing Criteria

Primary hyperaldosteronism with one of:

1. Presentation under the age of 30, OR
2. Family history of primary hyperaldosteronism or stroke below the age of 40

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Nephrology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R183.1	CYP11B1/CYP11B2 gene fusion Targeted variant testing	Singleton	Complex variant detection	Single interval	CYP11B1/CYP11B2 gene fusion	Targeted variant testing

R183糖皮质激素可治性醛固酮增多症(GRA)

检测标准

原发性醛固酮增多症，并具备以下之一：

1. 30岁以下发病，或
2. 原发性醛固酮增多症家族史或40岁以下卒中家族史

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 内分泌学
- 肾脏科

专科服务组

- 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R183.1	CYP11B1/CYP11B2 基因融合 靶向变异 检测	单人	复合体 变异 检测	单一区间	CYP11B1/CYP11B2 基因融合靶向变异	检测

R344 Primary hyperaldosteronism - KCNJ5

Testing Criteria

Primary hyperaldosteronism presenting under the age of 10 years

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Nephrology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R344.1	KCNJ5 Single gene sequencing	Singleton	Small variants	Single gene(s)	KCNJ5 (1380)	Single gene sequencing <10 amplicons

R344原发性醛固酮增多症-KCNJ5

检测标准

10岁前发病的原发性醛固酮增多症

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学
• 内分泌学
• 肾脏科

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R344.1	KCNJ5单基因测序	单人	小变异	单基因	KCNJ5 (1380)	单基因测序 <10扩增子

R160 Primary pigmented nodular adrenocortical disease

Testing Criteria

Primary pigmented nodular adrenocortical disease, OR

Clinical diagnosis of ACTH-independent Cushing syndrome of unknown aetiology.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R160.1	Primary pigmented nodular adrenocortical disease Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Primary pigmented nodular adrenocortical disease (566)	Small panel

R160原发性色素性结节性肾上腺皮质疾病

检测标准

原发性色素性结节性肾上腺皮质病，或

病因不明的ACTH非依赖性库欣综合征的临床诊断。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R160.1	原发性色素性结节性肾上腺皮质疾病小\panel	单人	小变异，拷贝数变异	基因检测板或基因座	原发性色素性结节性肾上腺皮质疾病 (566)	小检测板

R293 Albright hereditary osteodystrophy, pseudohypoparathyroidism pseudopseudohypoparathyroidism, acrodysostosis and osteoma cutis

Testing Criteria

Individuals with a clear clinical diagnosis of Albright hereditary osteodystrophy, pseudohypoparathyroidism or pseudopseudohypoparathyroidism, acrodysostosis and osteoma cutis based on clinical, radiological and/or biochemical assessment

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Paediatrics

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R293 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R293.1	Albright hereditary osteodystrophy, pseudohypoparathyroidism pseudopseudohypoparathyroidism, acrodysostosis and osteoma cutis Small panel	Singleton	Small variants, CNV	Panel of genes or loci	Albright hereditary osteodystrophy, pseudohypoparathyroidism pseudopseudohypoparathyroidism, acrodysostosis and osteoma cutis (1209)	Small panel
R293.2	GNAS DMRs Methylation testing	Singleton	Methylation, CNVs	Single interval	GNAS DMRs & STX16	Methylation testing

R293Albright遗传性骨营养不良，假性甲状旁腺功能减退症 假假性甲状旁腺功能减退症，肢端发育不全和骨瘤皮肤

检测标准

基于临床、影像学和/或生化评估，具有 Albright 遗传性骨营养不良、假性甲状旁腺功能减退症或假假性甲状旁腺功能减退症、肢端发育不全和皮肤骨瘤明确临床诊断的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 内分泌学
- 儿科

专科服务组

- 内分泌学

相关检测

请注意，对于 R293 临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

代码	名称	最佳家族结构	范围	目标类型目标名称		方法
R293.1	奥尔布赖特遗传性骨营养不良，假性甲状旁腺功能减退症 假假性甲状旁腺功能减退症，肢端发育不全和皮肤骨瘤 小检测板	Singleton	小检测板变异，拷贝数变异	检测板 基因或位点	假性甲状旁腺功能减退症 假性假甲状旁腺功能减退症，肢端发育不全和皮肤骨瘤 (1209)	小panel
R293.2 GNAS DMRs 甲基化测		单人	甲基化，拷贝数变异	单区间	GNAS DMRs与STX16	甲基化检测

R151 Familial hyperparathyroidism or Hypocalciuric hypercalcaemia

Testing Criteria

Familial Primary Hyperparathyroidism

i) <50y,

OR

ii) any age with

a) a confirmed or relevant family history, OR

b) multiglandular disease or hyperplasia in the presence of relevant family history, OR

c) parathyroid carcinoma or atypical or cystic adenoma, OR

d) ossifying fibroma(s) of the maxilla and /or mandible.

Hypocalciuric hypercalcaemia

Hypercalcaemia with hypocalciuria (calcium clearance: creatinine clearance ratio <0.02), usually with normal PTH

Overlapping indications

- R319 Calcium-sensing receptor phenotypes single gene test should be considered in neonatal hyperparathyroidism
- R217 and R218 Multiple endocrine neoplasia indications should be used where there are features of multiple endocrine neoplasia including hypercalcaemia
- R226 parathyroid carcinoma should be used for individuals with confirmed parathyroid carcinoma

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Surgery (head/neck/endocrine)
- Oncology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R151.1	Familial hyperparathyroidism or Hypocalciuric hypercalcaemia Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Familial hyperparathyroidism or Hypocalciuric hypercalcaemia (480)	Small panel

R151家族性甲状旁腺功能亢进症或低尿钙性高钙血症

检测标准

家族性原发性甲状旁腺功能亢进症

i) <50岁,或 ii) 任何年龄伴有

a) 已确认或相关的家族史，或

b) 存在相关家族史的多腺体疾病或增生，或

c) 甲状旁腺癌或非典型或囊性腺瘤，或

d) 上颌骨和/或下颌骨的骨化性纤维瘤。

低尿钙性高钙血症

高钙血症伴低尿钙(钙清除率：肌酐清除率比值<0.02),通常 PTH 正常

重叠指征

- R319 钙敏感受体表型单基因检测应考虑用于新生儿甲状旁腺功能亢进症
- 当存在多发性内分泌腺瘤病特征(包括高钙血症)时，应使用 R217 和 R218 多发性内分泌腺瘤病指征
- R226 甲状旁腺癌应用于确诊甲状旁腺癌的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 内分泌学
- 外科(头颈/内分泌)
- 肿瘤学

专科服务组

- 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R151.1	家族性甲状旁腺功能亢进症或低尿钙性高钙血症 小panel	单人	小变异，拷贝数变异	基因检测板或基因座	家族性甲状旁腺功能亢进症或低尿钙性高钙血症 (480)	小检测板

R153 Familial hypoparathyroidism

Testing Criteria

Non-syndromic hypoparathyroidism with low calcium levels and low or inappropriately normal serum PTH, with no detectable cause

Testing of patients who are normocalcaemic may occasionally be appropriate after consultation with an expert in calcium homeostasis

Overlapping indications

- R293 Albright hereditary osteodystrophy, pseudohypoparathyroidism and pseudopseudohypoparathyroidism test should be used where there is high clinical suspicion of one of these diagnoses

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R153.1	Familial hypoparathyroidism Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Familial hypoparathyroidism (312)	Small panel

R153家族性甲状旁腺功能减退症

检测标准

非综合征性甲状旁腺功能减退症，伴低钙水平及低或不适当正常的血清 PTH，无可检测的病因

对血钙正常患者的检测在咨询钙稳态专家后偶尔可能是适当的

重叠指征

• R293 Albright 遗传性骨营养不良、假性甲状旁腺功能减退症及
当临床高度怀疑上述诊断之一时，应使用假假性甲状旁腺功能减退症检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R153.1	家族性甲状旁腺功能减退症小panel	单人	小变异，拷贝数变异	基因检测板或基因座	家族性甲状旁腺功能减退症 (312)	小检测板

R154 Hypophosphataemia or rickets

Testing Criteria

Hypophosphataemia with no identifiable cause, with evidence of decreased renal phosphate reabsorption, which has or could lead to presentation with rickets.

OR

Low ALP AND one of the following:

- early dental loss
- rickets-like changes on X-ray
- chronic musculoskeletal pain
- atypical femoral fractures
- poor healing fractures

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R154.1	Hypophosphataemia or rickets Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Hypophosphataemia or rickets (482)	Small panel

R154低磷血症或佝偻病

检测标准

无可识别病因的低磷血症，伴肾磷酸盐重吸收减少的证据，已导致或可能导致佝偻病表现。或

低 ALP 且符合以下任一情况：

- 早期牙齿脱落
- X 线检查示佝偻病样改变
- 慢性肌肉骨骼疼痛
- 非典型股骨骨折
- 骨折愈合不良

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 内分泌学

专科服务组

- 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R154.1	低磷血症或佝偻病 小型检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	低磷血症或佝偻病 (482)	小检测板

R319 Calcium-sensing receptor phenotypes

Testing Criteria

1. Neonatal hyperparathyroidism, OR
2. Likely clinical diagnosis of autosomal dominant hypocalcaemia with hypercalciuria

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R319.1	CASR Single gene sequencing	Singleton	Small variants	Single gene(s)	CASR (1312)	Single gene sequencing >=10 amplicons

R319钙敏感受体表型

检测标准

1. 新生儿甲状旁腺功能亢进，OR

2. 可能临床诊断为常染色体显性低钙血症伴高尿钙

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R319.1	CASR单基因测序	单人	小变异	单基因	CASR (1312)	单基因测序 >=10扩增子

R157 IPEX - Immunodysregulation Polyendocrinopathy and Enteropathy, X-Linked

Testing Criteria

Males with type 1 diabetes mellitus in early infancy or childhood, AND ANY TWO of the features below, OR

Males with absent regulatory T cells, AND ONE of the features below:

- Hypothyroidism
- Severe enteropathy
- Eczema
- Autoimmune cytopenias
- One of the above 4 features plus a family history compatible with X-linked inheritance

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Gastroenterology
- Immunology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R157.1	FOXP3 Single gene sequencing	Singleton	Small variants	Single gene(s)	FOXP3 (1350)	Single gene sequencing >=10 amplicons

R157IPEX-免疫失调多内分泌腺病和肠病，X连锁

检测标准

婴儿早期或儿童期患 1 型糖尿病的男性，且具有以下特征中的任意两项，或调节性 T 细胞缺失的男性，且具有以下特征中的一项：

- 甲状腺功能减退症
- 严重肠病
- 湿疹
- 自身免疫性血细胞减少症
- 上述 4 项特征之一加上符合 X 连锁遗传的家族史

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 内分泌学
- 胃肠病学
- 免疫学

专科服务组

- 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R157.1	FOXP3单基因测序	单人	小变异	单基因	FOXP3 (1350)	单基因测序 >=10扩增子

R156 Carney complex

Testing Criteria

Two or more of the features from the list below (with histological confirmation where relevant), OR

One feature from the list below (with histological confirmation where relevant) and an affected first degree relative:

- Spotty skin pigmentation with typical distribution (lips, conjunctiva, vaginal and penile mucosa)
- Myxoma (cutaneous and mucosal)
- Cardiac myxomas
- Breast myxomatosis or fat-suppressed MRI suggestive of this finding
- PPNAD or paradoxical positive response of urinary glucocorticosteroid excretion to dexamethasone administration during Liddles test
- Acromegaly due to GH-producing adenoma
- Large cell calcifying Sertoli cell tumour (LDDST) or characteristic calcification on testicular ultrasound
- Thyroid carcinoma or multiple, hypoechoic nodules on thyroid ultrasound in a young patient
- Psammomatous melanotic schwannomas (PMS)
- Blue nevus, epithelioid blue nevus
- Breast ductal adenoma
- Osteochondromyxoma

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R156.1	PRKAR1A Single gene sequencing	Singleton	Small variants	Single gene(s)	PRKAR1A (1313)	Single gene sequencing >=10 amplicons

R156Carney复合征

检测标准

以下列表中的两项或以上特征(相关时经组织学确认)，或

符合以下列表中的一项特征(相关时需经组织学确认)以及一名患病的直系亲属：

- 具有典型分布的斑点状皮肤色素沉着(唇、结膜、阴道及阴茎黏膜)
- 黏液瘤(皮肤和黏膜)
- 心脏黏液瘤
- 乳腺黏液瘤病或脂肪抑制MRI提示该发现
- PPNAD 或尿糖皮质激素排泄对地塞米松的 paradoxical 阳性反应 Liddles试验期间的给药
- 因产生GH的腺瘤导致的肢端肥大症
- 大细胞钙化性 Sertoli 细胞肿瘤(LDDST)或睾丸超声上的特征性钙化
- 年轻患者中的甲状腺癌或甲状腺超声上的多个低回声结节
- 沙粒体性黑色素性神经鞘瘤(PMS)
- 蓝痣，上皮样蓝痣
- 乳腺导管腺瘤
- 骨软骨黏液瘤

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 皮肤病学
- 内分泌学

专科服务组

- 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R156.1	PRKAR1A单基因测序	单人	小变异	单基因	PRKAR1A (1313)	单基因测序 >=10扩增子

R148 Hypogonadotropic hypogonadism

Testing Criteria

Hypogonadotropic hypogonadism (absent or incomplete puberty with low LH/FSH in the context of low testosterone/oestradiol), with or without anosmia, with no detectable cause

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Gynaecology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R148.1	Hypogonadotropic hypogonadism	Singleton	Small variants, CNVs	Panel of genes or loci	Hypogonadotropic hypogonadism idiopathic (650)	Medium panel

R148低促性腺激素性性腺功能减退症

检测标准

低促性腺激素性性腺功能减退症(青春期缺失或不完全，伴低 LH/FSH 及低睾酮/雌二醇)，伴或不伴嗅觉缺失，未检测到明确病因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 内分泌学

• 妇科

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R148.1	低促性腺激素性性腺功能减退症	单人	小变异，拷贝数变异	基因检测板或基因座	低促性腺激素性特发性性腺功能减退症 (650)	中检测板

R159 Pituitary hormone deficiency

Testing Criteria

Biochemical evidence of deficiency of at least two pituitary hormones of neonatal or childhood onset.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R159.1	Pituitary hormone deficiency WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Pituitary hormone deficiency (483)	WES or Medium panel

R159垂体激素缺乏

检测标准

新生儿期或儿童期起病的至少两种垂体激素缺乏的生化证据。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R159.1	垂体激素缺乏症 WES 或中等 Panel	单人	小变异，拷贝数变异	基因检测板或基因座	垂体激素缺乏症 (483)	WES或Medium检测组合

R217 Endocrine neoplasia

Testing Criteria

Testing of individual (proband) affected with endocrine abnormalities where the individual +/- family history meets one of the following criteria:

1. Multiple endocrine neoplasia type 1 (MEN1). The proband has:
   a. Parathyroid multiglandular disease (hyperplasia/ adenomas) (<35 years), OR
   b. Any pituitary adenoma or insulinoma (< 20years), OR
   c. Pituitary macroadenoma (<30 years), OR
   d. ≥2 MEN1-related endocrine abnormalities (any age), OR
   e. ≥1 MEN1-related endocrine abnormality and ≥1 MEN1-related non-endocrine tumours (any age), OR
   f. ≥1 MEN1-related endocrine abnormality and a first degree relative has ≥1 MEN1-related endocrine abnormality

   MEN1-related endocrine abnormalities include:
   - Parathyroid hyperplasia/multiglandular adenomas
   - Pituitary tumors
   - Endocrine tumors of the gastro-entero-pancreatic (GEP) tract
   - Carcinoid tumors
   - Adrenocortical tumors

   MEN1-related non-endocrine tumours include:
   - facial angiofibromas
   - collagenomas
   - meningioma

2. Familial isolated pituitary adenoma (FIPA)

- Isolated pituitary adenoma developing under the age of 35, with at least one first degree relative with an isolated pituitary adenoma

3. X-linked acrogigantism

- Onset of excess of growth hormone diagnosed by age 20 years in male patients, with increased growth velocity and/or tall stature (height >2 standard deviations above the mean, or >3 standard deviations over mid-parental height)
- If testing on blood is negative and clinical suspicion of this diagnosis is strong, please contact the testing laboratory to discuss sending a fresh frozen tissue or skin biopsy sample to identify a mosaic form of the condition

NOTE: All cancers should be histologically confirmed

Where a patient doesn't meet the stated criteria but there is strong clinical suspicion of a monogenic predisposition to endocrine neoplasia, testing can go ahead after discussion in a specialist MDT meeting

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Surgery (head/neck/endocrine)
- Oncology

Specialist Service Group

- Endocrinology

R217内分泌肿瘤

检测标准

对患有内分泌异常的个体(先证者)进行检测，该个体 +/- 家族史

符合以下标准之一：

1. 多发性内分泌腺瘤病1型(MEN1)。先证者具有：
   a. 甲状旁腺多腺体疾病(增生/腺瘤)(<35岁),或
   b. 任何垂体腺瘤或胰岛素瘤(< 20岁),或
   c. 垂体大腺瘤(<30岁),或
   d. ≥2 MEN1相关内分泌异常(任何年龄)，或
   e. ≥1 项 MEN1 相关内分泌异常且 ≥1 项 MEN1 相关非内分泌肿瘤(任何年龄)，或
   f. ≥1 项 MEN1 相关内分泌异常且一名直系亲属有 ≥1 项 MEN1 相关内分泌异常

   MEN1 相关内分泌异常包括：- 甲状旁腺增生/多腺体腺瘤 - 垂体肿瘤

   - 胃-肠-胰(GEP)道内分泌肿瘤 - 类癌肿瘤 - 肾上腺皮质肿瘤

   MEN1 相关非内分泌肿瘤包括：- 面部血管纤维瘤 - 胶原瘤 - 脑膜瘤

2. 家族性孤立性垂体腺瘤(FIPA)

• 35 岁以下发生的孤立性垂体腺瘤，且至少有一名直系亲属患有孤立性垂体腺瘤

3. X连锁肢端巨人症

• 男性患者 20 岁前诊断的生长激素过多，伴生长速度加快和/或身材高大(身高 >2 个标准差高于均值，或 >3 个标准差高于中亲身高)

• 如果血液检测为阴性且临床高度怀疑该诊断，请联系检测实验室讨论送检新鲜冷冻组织或皮肤活检样本以识别该病的嵌合型

注：所有癌症均应经组织学确诊

如果患者不符合所述标准，但临床高度怀疑内分泌肿瘤的单基因易感性，可在专科 MDT 会议讨论后进行检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 内分泌学
• 外科(头颈/内分泌)
• 肿瘤学

专科服务组

• 内分泌学

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R217.1	Endocrine neoplasia Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Endocrine neoplasms (648)	Small panel

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R217.1	内分泌肿瘤 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	内分泌肿瘤（648）	小检测板

R223 Inherited phaeochromocytoma and paraganglioma excluding NF1

Testing Criteria

Testing of individual (proband) affected with cancer where the individual +/- family history meets one of the following criteria. The proband has:

1. Phaeochromocytoma <60 years, OR
2. Any paraganglioma OR metastatic phaeochromocytoma at any age, OR
3. Phaeochromocytoma / paraganglioma with loss of staining for SDH proteins on IHC, OR
4. Bilateral phaeochromocytoma (any age), OR
5. Phaeochromocytoma and renal cell carcinoma (any age), OR
6. Phaeochromocytoma / paraganglioma (any age) AND ≥1 relative (first / second / third degree relative) with phaeochromocytoma / paraganglioma / gastrointestinal stromal tumour

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

NOTE: Testing under this clinical indication does not include NF1

Overlapping indications

- R363 Inherited predisposition to GIST should be used where GIST is a prominent cancer type in the family
- M13 Phaeochromocytoma should be used for somatic testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R223.1	Inherited phaeochromocytoma and paraganglioma excluding NF1 Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Inherited phaeochromocytoma and paraganglioma excluding NF1 (649)	Small panel

R223遗传性嗜铬细胞瘤和副神经节瘤排除NF1

检测标准

对患有癌症的个体(先证者)进行检测，该个体 +/- 家族史符合以下标准之一。先证者具有：

1. 嗜铬细胞瘤<60 岁,或
2. 任何年龄的任何副神经节瘤或转移性嗜铬细胞瘤，或
3. 嗜铬细胞瘤/副神经节瘤伴 IHC 上 SDH 蛋白染色缺失，或
4. 双侧嗜铬细胞瘤(任何年龄)，或
5. 嗜铬细胞瘤和肾细胞癌(任何年龄)，或
6. 嗜铬细胞瘤/副神经节瘤(任何年龄)且 ≥1 名亲属(一级/二级/三级亲属)患有嗜铬细胞瘤/副神经节瘤/胃肠道间质瘤

注：先证者的癌症和家族中报告的大多数癌症应已得到确认注：本临床指征下的检测不包括 NF1

重叠指征

• R363 遗传性 GIST 易感性应在 GIST 为突出癌症类型的情况下使用
家族

• M13 嗜铬细胞瘤应用于体细胞检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R223.1	遗传性嗜铬细胞瘤及副神经节瘤排除NF1小panel	单人	小变异，拷贝数变异	基因检测板或基因座	遗传性嗜铬细胞瘤及副神经节瘤，除外NF1（649）	小检测板

R144 Congenital hyperinsulinism

Testing Criteria

Hypoglycaemia accompanied by one of the following, with no identifiable cause:

1. During an episode of hypoglycaemia there is a requirement for the glucose infusion to be at a rate of >8mg/kg/min, OR
2. Detectable serum insulin or c-peptide when the blood glucose is <3mmol/l, OR
3. Suppressed or undetectable serum fatty acids and ketone bodies

Where possible, clinicians are asked to submit samples from the probands parents for the DNA to be stored (R346) to allow follow-up of variants

Order of testing

- Start with ABCC8 and KCNJ11 single gene tests to determine surgical management
- Continue to panel test if negative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R144 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R144.1	ABCC8; KCNJ11	Singleton	Small variants,	Small panel	ABCC8; KCNJ11	Small panel
R144.2	Congenital hyperinsulinism Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Congenital hyperinsulinism (308)	Small panel

R144先天性高胰岛素血症

检测标准

低血糖伴以下任一情况，且无可识别病因：

1. 在低血糖发作期间，需要以 >8mg/kg/min 的速率进行葡萄糖输注，或
2. 血糖<3mmol/l时可检测到血清胰岛素或c肽,或
3. 血清脂肪酸和酮体被抑制或检测不到

在可能的情况下，请临床医生提交先证者父母的样本用于DNA储存(R346)，以便对变异进行随访

检测顺序

• 首先进行 ABCC8 和 KCNJ11 单基因检测，以确定手术方案

• 如果阴性，继续进行 panel 检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

请注意，对于 R144 临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R144.1	ABCC8; KCNJ11	单人	小变异，小检测板		ABCC8; KCNJ11	小检测板
R144.2	先天性高胰岛素血症小panel	单人	小变异，拷贝数变异	基因检测板或基因座	先天性高胰岛素血症(308) 小panel	

R158 Severe insulin resistance and lipodystrophy syndromes

Testing Criteria

Individuals with a clinical diagnosis of lipodystrophy with features likely to include lipoatrophy affecting the trunk, limbs and face, acromegaloid features, progeroid features, hepatomegaly, elevated serum triglycerides and severe insulin resistance with early development of diabetes,

AND

Acquired causes have been excluded

OR

Individuals with the following features of severe insulin resistance:

• Acanthosis nigricans

OR

• A fasting insulin >150pmol/l if not insulin treated OR if insulin treated an insulin requirement >3U/kg/day

AND

Are not obese (BMI <30kg/m2 if white (<95th centile for weight in children) or BMI <27kg/m2 (<95th centile for weight in children) if high prevalence type 2 diabetes group).

Overlapping indications

- R141 Monogenic diabetes test should be used for adult onset lipodystrophy with insulin resistance or diabetes
- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R158.1	Severe insulin resistance and lipodystrophy syndromes	Singleton	Small variants, CNVs	Panel of genes or loci	Lipodystrophy (546) New genes to be added to the panel: PIK3R1, WRN, BLM, ALMS1, PCNT, PCYT1A, , POC1A, MFN2, EPHX1, PSMB8, PSMB4	Medium panel

R158严重胰岛素抵抗和脂肪营养不良综合征

检测标准

临床诊断为脂肪营养不良的个体，其特征可能包括影响躯干、四肢和面部的脂肪萎缩、肢端肥大样特征、早老样特征、肝肿大、血清甘油三酯升高以及伴有糖尿病早期发展的严重胰岛素抵抗，

和

已排除获得性病因

或

具有以下严重胰岛素抵抗特征的个体:

• 黑棘皮病 OR

• 空腹胰岛素 >150pmol/l(若未接受胰岛素治疗)或若接受胰岛素治疗，胰岛素需求量 >3U/kg/天且

非肥胖(白人 BMI <30kg/m2(儿童体重<第95百分位)或高 prevalence 2型糖尿病群体 BMI <27kg/m2(儿童体重<第95百分位))。

重叠指征

• R141 单基因糖尿病检测应用于伴有胰岛素抵抗的成人起病脂肪营养不良，或
糖尿病

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R158.1	严重胰岛素抵抗和脂肪营养不良综合征	单人	小变异，拷贝数变异	基因检测板或基因座	脂肪营养不良 (546) 新基因将添加到panel: PIK3R1、WRN、BLM、ALMS1、PCNT、PCYT1A、POC1A、MFN2、EPHX	中检测板

R218 Multiple endocrine neoplasia type 2

Testing Criteria

Testing of individual (proband) affected with endocrine abnormalities where the individual +/- family history meets one of the following criteria. The proband has:

1. MTC (any age), OR
2. ≥2 MEN2-related endocrine abnormalities (any age), OR
3. ≥1 MEN2-related endocrine abnormality and a first degree relative with ≥1 MEN2-related endocrine abnormality

MEN2-related endocrine abnormalities include: Medullary Thyroid Carcinoma (MTC), Phaechromocytoma/paraganglioma, Parathyroid adenoma/hyperplasia, Hirschprungs disease

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

Overlapping indications

- R217 Endocrine neoplasia test should be used where a broader presentation is under investigation

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Surgery (head/neck/endocrine)
- Oncology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R218.1	RET Single gene sequencing	Singleton	Small variants	Single gene(s)	RET (1366)	Single gene sequencing >=10 amplicons

R218多发性内分泌肿瘤2型

检测标准

对患有内分泌异常的个体(先证者)进行检测，其中该个体 +/- 家族史符合以下标准之一。先证者具有：

1. MTC(任何年龄)，或
2. ≥2 MEN2相关内分泌异常(任何年龄)，或
3. ≥1 项 MEN2 相关内分泌异常，且一级亲属具有 ≥1 项 MEN2 相关内分泌异常

MEN2相关的内分泌异常包括：甲状腺髓样癌(MTC),
嗜铬细胞瘤/副神经节瘤、甲状旁腺腺瘤/增生、先天性巨结肠病

注：先证者的癌症以及家族中报告的大多数癌症应已得到确认

重叠指征

• R217 内分泌肿瘤检测应在调查更广泛表现时使用。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

通路中的位置

申请专科

• 临床遗传学
• 内分泌学
• 外科(头颈/内分泌)
• 肿瘤学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R218.1	RET单基因测序	单人	小变异	单基因	RET(1366)	单基因测序 >=10扩增子

R226 Inherited parathyroid cancer

Testing Criteria

Testing of individual (proband) affected with parathyroid carcinoma

NOTE: The probands tumour and majority of reported tumours in the family should have been confirmed

Overlapping indications

- R151 Familial hyperparathyroidism test should be used where benign forms of hyperparathyroidism are under investigation

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Surgery (head/neck/endocrine)
- Oncology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R226.1	CDC73 Single gene sequencing	Singleton	Small variants	Single gene(s)	CDC73 (1348)	Single gene sequencing >=10 amplicons

R226遗传性甲状旁腺癌

检测标准

先证者(proband)患甲状旁腺癌的检测

注：先证者的肿瘤以及家族中报告的大多数肿瘤应已得到确认

重叠指征

• R151 家族性甲状旁腺功能亢进症检测应在良性形式的甲状旁腺功能亢进症为正在调查中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 内分泌学
• 外科(头颈/内分泌)
• 肿瘤学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R226.1	CDC73单基因测序	单人	小变异	单基因	CDC73 (1348)	单基因测序 >=10扩增子

R162 Familial tumoral calcinosis

Testing Criteria

Individuals with a diagnosis of familial tumoral calcinosis, with or without hyperphosphataemia

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R162.1	Familial tumoral calcinosis Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Familial tumoral calcinosis (552)	Small panel

R162家族性肿瘤性钙化症

检测标准

诊断为家族性肿瘤性钙化的个体，伴或不伴高磷血症

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 内分泌学

专科服务组

• 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R162.1	家族性肿瘤性钙质沉着症 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	家族性肿瘤性钙化症(552) 小panel	

R417 Multi Locus Imprinting Disorder (MLID)

Testing Criteria

R417.1

A positive molecular diagnosis of an imprinting disorder resulting from, an imprinting disturbance (eg. Beckwith Wiedemann syndrome due to hypomethylation of KCNQ1OT1TSS-DMR (IC2) or Silver-Russell syndrome due to hypomethylation of H19-IGF2 IG-DMR (IC1), but not an imprinting disorder caused by a copy number variant or uniparental disomy

MILD testing may occasionally be appropriate in patients in whom an imprinting disorder is suspected, after expert clinical examination and discussion with Clinical Genetics, but where standard of care testing has not confirmed a molecular diagnosis.

R417.2

A positive molecular diagnosis of MLID: i.e. imprinting disturbance involving two or more imprinted loci. Sequencing must be performed on the proband and maternal sample for genes in panel R417.2.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- R143 Neonatal diabetes (ZFP57)

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Paediatrics
- Genomics Laboratory

Specialist Service Group

- Endocrinology

Associated Tests

Please note all the tests below will be undertaken for R417 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R417.1	Multi Locus Imprinting Disorder MLPA	Singleton	Methylation CNVs	Panel of genes or loci	genes on chromosomes: 6, 7, 11, 14, 15, 19, 20. (PLAGL1, GRB10, MEST, H19, KCNQ1, GTL2, SNRPN, PEG3, GNAS)	MS-MLPA
R417.2	Multi Locus Imprinting Disorder Small panel	Singleton	Small variants	Panel of genes or loci	Multi locus imprinting disorders (1109)	Small panel

R417多位点印记疾病(MLID)

检测标准 R417.1

由印记紊乱导致的印记疾病的阳性分子诊断(例如，由 KCNQ1OT1TSS-DMR(IC2) 低甲基化导致的 Beckwith Wiedemann 综合征或由 H19-IGF2 IG-DMR(IC1) 低甲基化导致的 Silver-Russell 综合征)，但不是由拷贝数变异或单亲二体导致的印记疾病

在疑似印记疾病的患者中，经过专家临床检查和与临床遗传学讨论后，但标准治疗检测尚未确认分子诊断时，MILD 检测偶尔可能适用。

R417.2

MLID 的阳性分子诊断：即涉及两个或更多印记位点的印记紊乱。必须对先证者和母源样本进行 panel R417.2 中基因的测序。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

• R143 新生儿糖尿病(ZFP57)

通路中的位置

申请专科

• 临床遗传学
• 内分泌学
• 儿科
• 基因组实验室

专科服务组

• 内分泌学

相关检测

请注意，对于 R417 临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R417.1	多基因座印记障碍 MLPA	单人	甲基化 拷贝数变异	基因检测板或基因座	染色体上的基因：6、7、11、14、15、19、20。（PLAGL1、GRB10、MEST、H19、KCNQ1、GTL2、SNRPN、PEG3、GNAS	MS-MLPA
R417.2	多基因座印记障碍 小panel	单人	小变异	基因检测板或基因座	多基因座印记障碍(1109)	小检测板

R440 Hereditary isolated diabetes insipidus

Testing Criteria

1. Biochemical features consistent with a diagnosis of diabetes insipidus (relevant biochemistry results and results of DDAVP testing, where appropriate, should be provided on the test request form to aid interpretation of the genetic results) AND
2. Exclusion of acquired causes of diabetes insipidus including primary polydipsia, trauma, malignancy, infection, autoimmune disease, drugs (eg. antibiotics, antifungals and antiviral agents)

Overlapping indications

- R198 Renal tubulopathies

Where in Pathway

At presentation

Requesting Specialties

- Nephrology
- Clinical Genetics

  Endocrinology

Specialist Service Group

- Endocrinology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R440.1	Hereditary isolated diabetes Insipidus small panel	Singleton	Small variants, CNVs	Panel of genes or loci	AVP, AVPR2, AQP2	Small panel

R440遗传性孤立性尿崩症

检测标准

1. 与尿崩症诊断一致的生化特征(相关生化结果
   以及适当时的 DDAVP 检测结果，应提供在检测申请单上，以帮助解释遗传结果)且

2.排除尿崩症的获得性原因，包括原发性烦渴、创伤、恶性肿瘤、
感染、自身免疫性疾病、药物(例如抗生素、抗真菌药和抗病毒药)

重叠指征

- R198 肾小管病

通路中的位置

就诊时

申请专科

- 肾脏科
- 临床遗传学

  内分泌学

专科服务组

- 内分泌学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R440.1	遗传性孤立性尿崩症 小panel	单人	小变异，拷贝数变异	基因检测板或基因座	AVP、AVPR2、AQP2	小检测板

Part V. Ophthalmology

R107 Bardet Biedl syndrome

Testing Criteria

Clinical features strongly indicative of a diagnosis of Bardet-Biedl syndrome including four or more primary features or three primary features and two or more secondary features:

1. Primary features:
   a. Retinal dystrophy
   b. Renal abnormalities
   c. Obesity
   d. Polydactyly
   e. Learning difficulties
   f. Hypogonadism in an individual assigned male at birth
2. Secondary features:
   a. Speech disorder/delay
   b. Strabismus/cataracts/astigmatism
   c. Brachydactyly/syndactyly
   d. Developmental delay
   e. Polyuria/polydipsia
   f. Ataxia/poor coordination/imbalance

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with overlapping or atypical presentations where features are not characteristic of Bardet-Biedl syndrome specifically

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Nephrology
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R107.1	Bardet Biedl syndrome	Singleton	Small variants, CNVs	Panel of genes or loci	Bardet Biedl syndrome (543)	Small panel

第V部分眼科学

R107BardetBiedl综合征

检测标准

强烈提示 Bardet-Biedl 综合征诊断的临床特征，包括四项或更多主要特征或三个主要特征和两个或更多次要特征：

1. 主要特征：
   a. 视网膜营养不良
   b. 肾脏异常
   c. 肥胖
   d. 多指(趾)
   e. 学习困难
   f. 出生时被指定为男性的个体中的性腺功能减退症
2. 次要特征：
   a. 言语障碍/发育迟缓
   b.斜视/白内障/散光 c.短指(趾)/并指(趾) d.发育迟缓
   e. 多尿/多饮
   f. 共济失调/协调不良/失衡

重叠指征

• 对于表现重叠或非典型、且特征并非特异性地符合Bardet-Biedl综合征的个体，应使用R27儿童期疾病或R89超罕见及非典型单基因疾病检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 肾脏科
• 眼科

专科服务组

• 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R107.1	巴德-毕德综合征	单人	小变异，拷贝数变异	基因检测板或基因座	Bardet Biedl综合征(543)	小检测板

R31 Bilateral congenital or childhood onset cataracts

Testing Criteria

Unexplained bilateral congenital or childhood onset cataracts

Overlapping indications

- R36 Structural eye disease test should be used in individuals with cataract in the context of microphthalmia or other structural eye disease
- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, after urine reducing substances

Where additional features are strongly suggestive of congenital infection, a TORCH screen should be performed before testing

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R31.3	Bilateral congenital or childhood onset cataracts WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Bilateral congenital or childhood onset Cataracts (230)	WGS

R31双侧先天性或儿童期起病白内障

检测标准

不明原因的双侧先天性或儿童期起病白内障

重叠指征

- 对于伴有白内障且存在以下情况的个体，应使用R36结构性眼病检测：
  小眼球或其他结构性眼病
- 对于存在先天性畸形、面容异常或其他复杂或综合征性表现的个体，应使用R27儿童期疾病或R89超罕见及非典型单基因疾病检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在尿还原物质检测后

若附加特征强烈提示先天性感染，应在检测前进行TORCH筛查

申请专科

- 临床遗传学
- 眼科

专科服务组

- 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R31.3	双侧先天性或儿童期起病白内障 WGS (phase 2)	三人组或单人	外显子水平CNVs，小变异	基因检测板或基因座	双侧先天性或儿童期起病 白内障 (230)	全基因组测序

R32 Retinal disorders

Testing Criteria

Unexplained retinal disease that is likely to be monogenic

Please note: for retinal hamartoma please use other more appropriate Clinical Indications for testing where the patient meets the eligibility criteria, for example, R221 Familial tumours of the nervous system (as NF2 is not included on the retinal disorders panel) or R228 Tuberous sclerosis (as TSC1 & TSC2 are not included on the retinal disorders panel).

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations
- R33 X-linked retinitis pigmentosa test should be used where features are consistent with X-linked retinitis pigmentosa

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant Ophthalmologist expert in inherited eye disease

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R32.2	Retinal disorders WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Retinal disorders (307)	WGS

R32视网膜疾病

检测标准

疑似单基因遗传的不明原因视网膜疾病

请注意：对于视网膜错构瘤，若患者符合检测资格标准，请使用其他更合适的临床指征进行检测，例如R221神经系统家族性肿瘤(因NF2未纳入视网膜疾病检测 panel)或R228结节性硬化症(因TSC1和TSC2未纳入视网膜疾病检测 panel)。

重叠指征

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
存在先天性畸形、面容异常或其他复杂或综合征性表现的个体 • 对于特征符合X连锁视网膜色素变性的个体，应使用R33 X连锁视网膜色素变性检测
色素变性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经遗传性眼病专家顾问眼科医师评估后 申请专科

• 临床遗传学

• 眼科

专科服务组

• 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R32.2	视网膜疾病 WGS(第二阶段)	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	视网膜疾病 (307)	全基因组测序

R33 Possible X-linked retinitis pigmentosa

Testing Criteria

Unexplained retinal disease with features consistent with X-linked retinitis pigmentosa in whom variants at RPGR exon ORF15 have not been excluded

Order of testing

- RPGR exon ORF15 to be analysed first and if uninformative, consider R32 WGS

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant Ophthalmologist expert in inherited eye disease

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R33.1	RPGR exon ORF15 Targeted variant testing	Singleton	Small variants	Single interval	RPGR exon ORF15	Targeted variant testing

R33疑似X连锁视网膜色素变性

检测标准

原因不明的视网膜疾病，特征符合X连锁视网膜色素变性，且未排除RPGR外显子ORF15变异

检测顺序

• 首先分析 RPGR exon ORF15，若无信息，则考虑 R32 WGS

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经遗传性眼病专家顾问眼科医师评估后

申请专科

• 临床遗传学

• 眼科

专科服务组

• 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R33.1	RPGR外显子ORF15靶向变异检测	单人	小变异	单一区间	RPGR外显子ORF15	靶向变异检测

R36 Structural eye disease

Testing Criteria

1. Microphthalmia or anophthalmia or uveoretinal coloboma where there is evidence to support a likely monogenic cause, for example bilateral disease, consanguinity or additional ocular and non-ocular features, OR
2. Unilateral or bilateral congenital / developmental glaucoma, OR
3. Bilateral developmental glaucoma or anterior segment malformation, except where there is evidence of a non-genetic cause, OR
4. Aniridia with family history

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations
- R38 Sporadic aniridia test should be used instead for sporadic classical aniridia

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant Ophthalmologist. Cases with multiple malformations or syndromic features should have been discussed with a Consultant Clinical Geneticist.

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R36.2	Structural eye disease WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Structural eye disease (509)	WGS

R36结构性眼病

检测标准

1. 小眼球或无眼球或葡萄膜视网膜缺损，且有证据支持可能的单基因病因，例如双侧病变、近亲婚配或附加眼部及非眼部特征，或
2. 单侧或双侧先天性/发育性青光眼，或
3. 双侧发育性青光眼或前节畸形，除非有证据表明为非遗传性病因，或
4. 无虹膜症伴家族史

重叠指征

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于存在先天性畸形、面容异常或其他复杂或综合征性表现的个体

• 对于散发性典型无虹膜，应改用R38散发性无虹膜检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经顾问眼科医师评估后。存在多发畸形或综合征性特征的病例应已与顾问临床遗传学家讨论。

申请专科

• 临床遗传学

• 眼科

专科服务组

• 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R36.2	结构性眼疾病 WGS (第2阶段)	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	结构性眼病 (509)	全基因组测序

R38 Sporadic aniridia

Testing Criteria

Sporadic classical bilateral aniridia including those with features suggestive of WAGR syndrome.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Oncology
- Clinical Genetics
- Ophthalmology
- Paediatrics

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R38.2	Sporadic aniridia Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Sporadic aniridia (510)	Small panel

R38散发性无虹膜症

检测标准

散发性典型双侧无虹膜，包括具有提示WAGR综合征特征的病例。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 肿瘤学
- 临床遗传学
- 眼科
- 儿科

专科服务组

- 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R38.2	散发性无虹膜 小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	散发性无虹膜 (510)	小检测板

R39 Albinism or congenital nystagmus

Testing Criteria

1. Albinism or generalised cutaneous hypopigmentation with or without ocular involvement, OR
2. Unexplained congenital nystagmus without a causative lesion on MRI brain

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant Ophthalmologist (for ophthalmic presentations)

Requesting Specialties

- Clinical Genetics
- Dermatology
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R39.1	Albinism or congenital nystagmus WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Albinism or congenital nystagmus (511)	WES or Medium panel

R39白化病或先天性眼球震颤

检测标准

1. 白化病或全身性皮肤色素减退，伴或不伴眼部受累，或
2. 不明原因的先天性眼球震颤，脑部MRI未见致病性病变

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经顾问眼科医师评估后(针对眼科表现)

申请专科

- 临床遗传学
- 皮肤病学
- 眼科

专科服务组

- 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R39.1	白化病或先天性眼震 WES 或 Medi	单人	小变异，拷贝数变异	基因检测板或基因座	白化病或先天性眼球震颤 (511)	WES或Medium检测组合

R41 Optic neuropathy

Testing Criteria

Unexplained optic neuropathy

Overlapping indications

- R42 Leber hereditary optic neuropathy test should be used where clinical features are consistent with Leber hereditary optic neuropathy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following expert by a Consultant Ophthalmologist

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Please note all the tests below will be undertaken for R41 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R41.1	Optic neuropathy WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Optic neuropathy (186)	WES or Medium panel
R41.3	Optic neuropathy	Singleton	Targeted variant testing	Three common LHON variants	Three common LHON variants	Targeted variant testing

R41视神经病

检测标准

不明原因视神经病变

重叠指征

• 对于临床特征符合Leber遗传性视神经病的个体，应使用R42 Leber遗传性视神经病检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

由顾问眼科医师中的专家接诊时

申请专科

• 临床遗传学

• 眼科

专科服务组

• 眼科

相关检测

请注意，对于R41临床指征申请，将进行以下所有检测，除非临床表现和/或初步结果提示所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R41.1	视神经病 WES或Medium 检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	视神经病 (186)	WES或Medium 检测组合
R41.3	视神经病	单人	靶向 变异检测	三种常见 LHON变异	三种常见LHON变异	靶向变异 检测

R43 Blepharophimosis ptosis and epicanthus inversus

Testing Criteria

Clinical features indicative of a likely clinical diagnosis of blepharohimosis, ptosis and epicanthus inversus syndrome (BPES) including the presence of all of the following: blepharophimosis, ptosis, epicanthus inversus AND telecanthus

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Please note all the tests below will be undertaken for R43 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R43.1	FOXL2 Single gene sequencing	Singleton	Small variants	Single gene(s)	FOXL2 (1310)	Single gene sequencing <10 amplicons
R43.2	FOXL2 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	FOXL2 (1310)	MLPA or equivalent
R43.3	FOXL2 STR testing	Singleton	STRs	Single gene(s)	FOXL2 STR (1310)	STR testing

R43睑裂狭小上睑下垂和内眦赘皮倒转

检测标准

临床特征提示可能临床诊断为睑裂狭小、上睑下垂和内眦赘皮倒转综合征(BPES)，包括存在以下所有表现：睑裂狭小、上睑下垂、内眦赘皮倒转 AND 内眦间距增宽

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 眼科

专科服务组

• 眼科

相关检测

请注意，对于R43临床指征申请，将进行以下所有检测，除非临床表现和/或初步结果提示所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R43.1	FOXL2单基因测序	单人	小变异	单基因	FOXL2 (1310)	单基因测序 <10扩增子
R43.2	FOXL2 MLPA或等效	单人	外显子水平拷贝数变异	单基因	FOXL2 (1310)	MLPA或等效
R43.3	FOXL2 短串联重复序列检测	单例	短串联重复序列	单基因	FOXL2 STR (1310)	短串联重复序列检测

R46 Congenital fibrosis of the extraocular muscles

Testing Criteria

Individuals with a suspected clinical diagnosis of congenital fibrosis of the extraocular muscles

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R46.1	Congenital fibrosis of the extraocular muscles Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Congenital fibrosis of the extraocular muscles (512)	Small panel

R46先天性纤维化的眼外肌

检测标准

疑似临床诊断为先天性眼外肌纤维化的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 神经科

• 眼科

专科服务组

• 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R46.1	先天性纤维化眼外的肌肉小panel	单人	小变异，拷贝数变异	基因检测板或基因座	先天性纤维化眼外肌 (512)	小检测板

R262 Corneal dystrophy

Testing Criteria

Corneal dystrophy of likely monogenic aetiology

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant Ophthalmologist expert in inherited eye disease

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R262.1	Corneal dystrophy WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Corneal dystrophies (658)	WES or Medium panel

R262角膜营养不良

检测标准

可能为单基因病因的角膜营养不良

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经遗传性眼病专家顾问眼科医师评估后

申请专科

• 临床遗传学

• 眼科

专科服务组

• 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R262.1	角膜营养不良 WES或Medium 检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	角膜营养不良 (658)	WES或Medium 检测组合

R45 Stickler syndrome

Testing Criteria

Clinical features indicative of likely Stickler syndrome

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation and/or as part of clinical assessment for the Stickler Highly Specialised Service

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R45.1	Stickler syndrome Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Stickler syndrome (3)	Small panel

R45Stickler综合征

检测标准

提示可能为 Stickler 综合征的临床特征

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时和/或作为 Stickler 高度专业化服务临床评估的一部分

申请专科

• 临床遗传学

• 眼科

专科服务组

• 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R45.1	Stickler综合征 小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	Stickler综合征(3)	小检测板

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R420 Pseudoxanthoma elasticum

Testing Criteria

Individuals who have characteristic features of Pseudoxanthoma elasticum:

- Papules or plaques on the skin of the neck and/or flexural creases (antecubital fossae, axillae, groin, or popliteal fossae) and/or calcified dystrophic elastic fibres on biopsied skin using a von Kossa or similar stain) AND/OR
- Retinal finding (angioid streaks, *peau d'orange*, or choroidal vascularization).

Overlapping indications

- R384 Generalised arterial calcification in infancy

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Ophthalmology

Specialist Service Group

- Ophthalmology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R420.1	Pseudoxanthoma elasticum	Singleton	Small variants, CNVs	Panel of genes or loci	ABCC6, ENPP1 (1381)	Small panel

R420弹性假黄瘤

检测标准

具有弹性假黄瘤特征性表现的个体：

- 颈部和/或屈侧皱褶处(肘前窝、腋窝、腹股沟、或腘窝)皮肤上的丘疹或斑块，和/或活检皮肤使用 von Kossa 或类似染色显示钙化性营养不良弹性纤维)和/或
- 视网膜发现(血管样条纹、橘皮样或脉络膜血管化)。

重叠指征

- R384 婴儿期全身性动脉钙化

通路中的位置

申请专科

- 临床遗传学
- 眼科

专科服务组

- 眼科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R420.1	假性黄色瘤 弹性纤维	单人	小变异， 拷贝数变异	基因检测板或 基因座	ABCC6、ENPP1 (1381)	小检测板

Part VI. Fetal (including NIPD)

R401 Common aneuploidy testing - prenatal

Testing Criteria

Prenatal findings requiring common aneuploidy testing including:

1. abnormal first trimester combined screening, OR
2. characteristic findings of a common aneuploidy on ultrasound scan

Overlapping indications

- R22 Fetus with a likely chromosomal abnormality, OR
- R21 Fetus with a likely genetic cause

tests should be used where additional copy number of sequence analysis is required

Where in Pathway

N/A

Requesting Specialties

- Clinical Genetics
- Fetal Medicine
- Obstetrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R401.1	Genomewide Common aneuploidy testing – prenatal	Singleton	Aneuploidy	Genomewide	Genomewide	Common aneuploidy testing

第VI.胎儿(包括NIPD)

R401常见非整倍体检测-产前

检测标准

需要常见非整倍体检测的产前发现，包括：1. 孕早期联合筛查异常，或

2. 超声扫描中常见非整倍体的特征性表现

重叠指征

• R22 胎儿可能存在染色体异常，或

• R21 胎儿可能存在遗传学病因

在需要额外拷贝数序列分析时应使用检测

通路中的位置

申请专科

• 临床遗传学

• 胎儿医学

• 产科

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R401.1	全基因组范围常见非整倍体检测 - 产前	单人	非整倍体	全基因组范围	全基因组范围	常见非整倍体检测

R445 T21, T18 and T13 aneuploidy testing - NIPT (previous history)

Testing Criteria

Any previous pregnancy with reported full trisomy of chromosomes 21 (Down's syndrome), 18 (Edwards' syndrome) and 13 (Patau's syndrome), meeting the following criteria:

Inclusion:

- From 10 weeks (gestational age confirmed by dating scan) and up to 21 weeks and 6 days (21+6) of pregnancy.
- Two attempts at NIPT per pregnancy can be offered.
- In both singleton and twin pregnancies

Exclusion:

- Maternal cancer (unless in remission)
- Blood transfusion in the last 4 months (whole blood or plasma)
- Bone marrow or organ transplant recipient
- Vanished twin pregnancy (an empty second pregnancy sac or a second pregnancy sac containing non-viable fetus)
- Maternal T21
- Maternal balanced translocation or mosaicism of T21, T18 or T13
- Immunotherapy in the current pregnancy, excluding IVIg treatment
- Stem cell therapy
- Previous pregnancy was not a full trisomy (reciprocal translocation or partial trisomy)
- The current pregnancy was conceived using a donor egg (unless the egg for this pregnancy is from the same egg donor used in a previous pregnancy diagnosed with Down's, Edward's or Patau's syndrome)

Eligibility criteria that require discussion - Contact the laboratory before taking a NIPT sample when there is a history of:

- Maternal cancer in the current pregnancy.
- Immunotherapy in the current pregnancy using medication, such as Neupogen, which introduces additional genomic material into the bloodstream.
- Any other maternal chromosomal condition other than T21, T18 or T13.

Overlapping indications

- R401 Common aneuploidy testing – prenatal should be used where amniocentesis or Chorionic villus sampling (CVS) taken.
  - R470 T21, T18 and T13 aneuploidy testing – NIPT NHS Fetal Anomaly Screening Programme (FASP), should be used if NIPT is being offered as part of the NHS FASP programme

Where in Pathway

Samples to be taken by trained midwife or Clinical Genetics Unit and sent directly to the testing laboratory using the same sample referral routes as per the Fetal Anomaly Screening Programme.

Requesting Specialties

- Clinical Genetics
  - Specialist Midwifery

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R445.1	T13, T18 & T21 aneuploidy testing NIPT (previous history)	Singleton	Aneuploidy	Chromosome 13, 18 and 21	Chromosomes 13, 18 and 21	NIPT

R445T21、T18和T13非整倍体检测-NIPT(既往史)

检测标准

任何既往妊娠报告为 21 号染色体(唐氏综合征)、18 号染色体(爱德华兹综合征)和 13 号染色体(帕陶综合征)完全三体，且符合以下标准：

包含：

- 从 10 周(经孕龄扫描确认的孕龄)至 21 周 6 天(21+6)妊娠期。
- 每次妊娠可提供两次 NIPT 尝试。
- 在单胎和双胎妊娠中

排除：

- 母体癌症(除非处于缓解期)
- 过去4个月内接受过输血(全血或血浆)
- 骨髓或器官移植受者
- 消失双胎妊娠(空第二妊娠囊或第二妊娠囊含不可存活胎儿)
- 母体 T21
- 母源平衡易位或 T21、T18 或 T13 嵌合体
- 本次妊娠期间接受免疫治疗，不包括 IVIg 治疗
- 干细胞治疗
- 既往妊娠不是完全三体(相互易位或部分三体)
- 本次妊娠使用供卵受孕(除非本次妊娠的卵子来自既往诊断为唐氏、爱德华兹或帕陶综合征妊娠所使用的同一供卵者)

需要讨论的检测资格标准 - 在采集 NIPT 样本前联系实验室，当

- 本次妊娠期间母体患癌。
- 本次妊娠期间使用药物进行免疫治疗，例如 Neupogen，其引入额外的基因组物质进入血流。
- 除 T21、T18 或 T13 以外的任何其他母体染色体状况。

重叠指征

- 当进行羊膜穿刺术或绒毛膜绒毛取样时，应使用 R401 常见非整倍体检测 - 产前取样(CVS)已采集。
  - 如果 NIPT 作为 NHS FASP 项目的一部分提供，应使用 R470 T21、T18 和 T13 非整倍体检测 - NIPT NHS 胎儿异常筛查项目(FASP)

通路中的位置

样本应由受过培训的助产士或临床遗传学单位采集，并按照胎儿异常筛查项目的相同样本转诊途径直接送至检测实验室。

申请专科

- 临床遗传学
  - 专科助产

专科服务组

- 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R445.1 T13、T18 和 T21	非整倍体检测 NIPT(既往)病史）	单人	非整倍体	13号染色体，18和21	13、18 和 21 号染色体	NIPT

R470 T21, T18 and T13 aneuploidy testing – NIPT NHS Fetal Anomaly Screening Programme (FASP)

Testing Criteria

Test for Down's syndrome (Trisomy 21), Edwards' syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13) as part of the NHS FASP pathway.

Any current pregnancy with a higher chance screening result from the NHS FASP combined or quadruple test. A higher chance result is greater than or equal to 1 in 150 at term (between 1 in 2 and 1 in 150). The following criteria must be met:

Inclusions:

- A higher chance result for T21 or a joint higher chance result for T18 and T13 from the NHS combined test
- A higher chance result for T21 *(and T18 following implementation)* from the NHS quadruple test
- In both singleton and twin pregnancies
- Up to 21 weeks and 6 days (21+6) of pregnancy
- In an in-vitro fertilisation (IVF) or donor egg pregnancy

Exclusions:

- A lower chance result for T21, T18 or T13 from the NHS combined or NHS quadruple test
  To note: where there is a history of a previous pregnancy with T21, T18 or T13, please request the test for T21, T18, T13 aneuploidy testing – NIPT (previous history) (using code R445) where the patient meets the criteria.
- In higher multiple pregnancies (triplets or more)
- After 21+6 weeks of pregnancy
- Blood transfusion in the last 4 months (whole blood or plasma)
- Bone marrow or organ transplant recipient
- Stem cell therapy
- Vanished twin pregnancy (an empty second pregnancy sac or a second pregnancy sac containing non-viable fetus)
- Maternal T21 or mosaicism of T21, T18 or T13
- Maternal balanced translocation involving chromosomes 21, 18 or 13

Eligibility criteria requiring discussion

Contact the laboratory before taking a NIPT sample when there is a history of:

- Maternal cancer in the current pregnancy.
- Immunotherapy in the current pregnancy using medication, such as Neupogen, which introduces additional genomic material into the bloodstream.
- Any other maternal chromosomal condition other than T21, T18 or T13.

Overlapping indications

- R401 Common aneuploidy testing – prenatal, should be used where amniocentesis or Chorionic villus sampling (CVS) is taken
- R445 T21, T18 and T13 aneuploidy testing – NIPT (previous history), should be used where any previous pregnancy was reported full trisomy of chromosomes 13, 18 or 21.

R470T21、T18和T13非整倍体检测-NIPTNHS胎儿异常筛查项目(FASP)

检测标准

作为 NHS FASP 路径的一部分，检测唐氏综合征(21 三体)、爱德华兹综合征(18 三体)和帕陶综合征(13 三体)。

任何本次妊娠 NHS FASP 联合或四联试验筛查结果为较高几率。较高几率结果为足月时大于或等于 1/150(介于 1/2 和 1/150 之间)。该
必须满足以下标准：

包含：

- 来自 NHS 的 T21 较高几率结果或 T18 和 T13 联合较高几率结果
  联合检测
- 来自 NHS 四联试验的 T21 *(*以及实施后的 *T18)*较高几率结果
- 在单胎和双胎妊娠中
- 妊娠至 21 周零 6 天(21+6)
- 在体外受精(IVF)或供卵妊娠中

排除：

- 来自 NHS 联合或 NHS 四联试验的 T21、T18 或 T13 较低几率结果
  注意：若既往有 *T21*、*T18* 或 *T13* 妊娠史，且患者符合标准，请申请 *T21*、*T18*、*T13* 非整倍体检测 - *NIPT(*既往史*)(*使用代码 *R445)*。
- 在高阶多胎妊娠(三胎或以上)中
- 妊娠21+6周后
- 过去4个月内接受过输血(全血或血浆)
- 骨髓或器官移植受者
- 干细胞治疗
- 消失双胎妊娠(空第二妊娠囊或第二妊娠囊含非存活胎儿)
- 母体 T21 或 T21、T18 或 T13 的嵌合体
- 涉及染色体21、18或13的母源平衡易位

需要讨论的资格标准

在有以下病史时，采集 NIPT 样本前请联系实验室：

- 本次妊娠期间母体患癌。
- 本次妊娠期间使用药物进行免疫治疗，例如 Neupogen，其引入额外的基因组物质进入血流。
- 除 T21、T18 或 T13 以外的任何其他母体染色体状况。

重叠指征

- R401 常见非整倍体检测 - 产前，应在进行羊膜腔穿刺或绒毛膜绒毛取样(CVS)时使用
- R445 T21、T18 和 T13 非整倍体检测 - NIPT(既往史)，应在报告既往任何妊娠为染色体 13、18 或 21 完全三体时使用。

Where in Pathway

Samples to be taken by an appropriately trained healthcare professional following a discussion about the patient's results. Samples to be sent directly to the testing laboratory in line with the sample referral routes as per NHS FASP.

Requesting Specialties

- Midwifery
- Fetal medicine
- Obstetrics

Specialist Service Group

Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R470.1	T13, T18 & T21 aneuploidy testing NIPT NHS FASP	Singleton	Aneuploidy	Chromosome 13, 18 and 21	Chromosomes 13, 18 and 21	NIPT

通路中的位置

样本应由经过适当培训的医疗专业人员在讨论患者结果后采集。样本应按照 NHS FASP 的样本转诊途径直接送至检测实验室。

申请专科

- 助产
- 胎儿医学
- 产科

专科服务组

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R470.1 T13、T18 和 T21	非整倍体检测 NIPT NHS FASP	单人	非整倍体	13号染色体，18和21	13、18 和 21 号染色体	NIPT

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R318 Recurrent miscarriage with products of conception available for testing

Testing Criteria

Recurrent miscarriage with products of conception available for testing – defined as three or more miscarriages.

Overlapping indications

- R464 Recurrent miscarriage where products of conception are not available for testing - parental karyotype
- R22 Fetus with a likely chromosomal abnormality, should be used in:
  - cases of isolated miscarriage with additional features suggestive of chromosome abnormality
  - cases of third trimester intrauterine death or still birth in the absences of other likely causes
- R27 Paediatric disorders or R412 Fetal anomalies with a likely genetic cause - non urgent, should be used in cases of fetal anomaly with likely genetic cause

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Fetal Medicine
- Gynaecology
- Obstetrics

Specialist Service Group

- Core

Associated Tests

Please note all the tests below will be undertaken for R318 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R318.1	Genomewide Common aneuploidy testing - miscarriage	Singleton	Aneuploidy	Genomewide	Genomewide	Common aneuploidy testing
R318.2	Genomewide Microarray	Singleton	Genomewide CNVs	Genomewide	Genomewide	Microarray

R318复发性流产伴妊娠产物可供检测检测

检测标准

复发性流产且妊娠产物可供检测 - 定义为三次或以上流产。

重叠指征

- R464 复发性流产且妊娠产物不可供检测 - 父母核型分析
- R22 胎儿可能存在染色体异常，应用于：
  - 孤立性流产病例，伴有提示染色体异常的额外特征
  - 妊娠晚期宫内死亡或死产病例，且无其他可能原因
- R27 儿科疾病或 R412 可能具有遗传原因的胎儿异常 - 非紧急，应用于存在可能遗传原因的胎儿异常病例

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 胎儿医学
- 妇科
- 产科

专科服务组

- 核心

相关检测

请注意，以下所有检测将针对 R318 临床指征申请进行，除非临床表现和/或初始结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R318.1	全基因组范围常见非整倍体检测--流产	单人	非整倍体	全基因组范围	全基因组范围	常见非整倍体检测
R318.2	全基因组范围微阵列（基因芯片）	单人	全基因组范围拷贝数变异	全基因组范围	全基因组范围	微阵列（基因芯片）

R22 Fetus with a likely chromosomal abnormality

Testing Criteria

This indication is relevant to:

- ongoing pregnancies OR
- where there has been fetal loss, termination of pregnancy or miscarriage, accompanied by additional features suggestive of chromosome abnormality OR
- intrauterine death or stillbirth from 24 weeks and in the absence of other likely causes

Overlapping indications

- R401 Common aneuploidy testing – prenatal or R26 Likely common aneuploidy should be used where only common aneuploidy testing is indicated
- R21 Fetal anomalies with a likely genetic cause test should be used where it is considered more appropriate and following discussion with a Clinical Geneticist
- R318 Recurrent miscarriage with products of conception available for testing can be used where there has been recurrent miscarriage in the absence of additional features suggestive of chromosomal abnormality
- R27 Paediatric disorders or R412 Fetal anomalies with a likely genetic cause - non urgent, should be used for non-urgent testing (e.g. where there is miscarriage, imminent fetal loss, or termination of pregnancy) in cases of fetal anomaly with likely genetic cause

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Fetal Medicine
- Pathology

Specialist Service Group

- Core

Associated Tests

Please note all the tests below will be undertaken for R22 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R22.1	Genomewide Common aneuploidy testing – prenatal	Singleton	Aneuploidy	Genomewide	Genomewide	Common aneuploidy testing
R22.2	Genomewide Microarray	Singleton	Genomewide CNVs	Genomewide	Genomewide	Microarray

R22胎儿伴可能染色体异常

检测标准

该适应证适用于：

• 持续妊娠或

• 在发生胎儿丢失、终止妊娠或流产，并伴有额外提示染色体异常的特征或 • 自 24 周起的宫内死亡或死产，且无其他可能原因

重叠指征

• R401 常见非整倍体检测 - 产前或 R26 可能常见非整倍体应在仅指示进行常见非整倍体检测

• R21 可能具有遗传原因的胎儿异常检测应在认为更合适时并在与临床遗传学家讨论后使用

• R318 复发性流产且妊娠产物可供检测可用于复发性流产且无提示染色体异常的额外特征时

• R27 儿科疾病或 R412 可能具有遗传原因的胎儿异常 - 非紧急，应用于非紧急检测(例如在发生流产、即将发生的胎儿丢失或终止妊娠时)，适用于可能具有遗传原因的胎儿异常病例

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 胎儿医学

• 病理学

专科服务组

• 核心

相关检测

请注意，以下所有检测将针对 R22 临床指征申请进行，除非临床表现和/或初始结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R22.1	全基因组范围常见非整倍体检测 - 产前	单人	非整倍体	全基因组范围	全基因组范围	常见非整倍体检测
R22.2	全基因组范围微阵列（基因芯片）	单人	全基因组范围拷贝数变异	全基因组范围	全基因组范围	微阵列（基因芯片）

R21 Fetal anomalies with a likely genetic cause

Testing Criteria

For more detailed guidance for R21 outlined in the fetal whole exome service guidance documentation please contact your local Genomic Laboratory Hub.

Fetus with multiple major structural abnormalities detected on fetal ultrasound where multidisciplinary review to include clinical genetics, tertiary fetal medicine specialists, clinical scientists and, where appropriate, relevant paediatric specialists considers a monogenic malformation disorder is likely

This indication is relevant in ongoing pregnancies where a genetic diagnosis may influence management of the ongoing pregnancy and NOT where there is imminent fetal loss or termination of pregnancy, or miscarriage has already occurred

NOTE: This indication is for use when rapid/urgent testing is required. Please use R412 for non-urgent testing

Clinical examples

• Fetuses with multiple anomalies, suspected skeletal dysplasias (IUGR should be excluded), large echogenic kidneys with a normal bladder, major CNS abnormalities (excluding neural tube defects), multiple contractures (excluding isolated bilateral talipes).
• Nuchal translucency measured between 11 and 14 weeks gestation of greater than 6.5mm plus another anomaly (that can include a minor finding) with a normal array CGH
• Isolated non-immune fetal hydrops (detected at or after the routine 18-20-week scan in the second or third trimesters), defined as fluid/oedema in at least two compartments (e.g. skin, pleural, pericardial or ascites) with a normal array CGH
• Persistent nuchal translucency (>3.5mm) can only be considered in the presence of other structural abnormalities in two or more systems.
• Minor 'markers of aneuploidy' – choroid plexus cysts, echogenic foci, mild renal pelvis dilation, small nasal bone, long bones on 3rd centile etc are excluded.
• Mild ventriculomegaly should only be considered as an abnormality if the posterior horn is persistently >11mm on two or more scans. Under these circumstances it is not considered a major CNS abnormality in isolation
• Abnormality of the corpus callosum, either partial or complete agenesis – either in isolation or with other anomalies
• Pregnancies of consanguineous couples that do not strictly fulfil the above criteria, but where a monogenic disorder is considered likely
• Recurrences of particular fetal anomalies in pregnancies of the same couple that do not strictly fulfil the above criteria, but where a monogenic disorder is considered likely due to the recurrence. Neural tube defects excluded

The two criteria below can be considered as eligibility criteria alone or in association with other major abnormalities. Requests will not be actioned without having doppler evidence.

- Small for gestational age can be considered as eligible for R21 under the following circumstances; all measurements <3rd percentile with a confirmed early ultrasound estimated date of delivery (EDD) scan, including abdominal circumference (AC) and head circumference (HC), and no evidence of placental insufficiency including normal fetal and maternal dopplers, no history of previous FGR, PAPP-A (if measured) not low, no maternal history of SLE etc and no past obstetric history of FGR or still birth.
- Isolated short long bones can be considered as an abnormality and eligible for R21 under the following circumstances; all long bones <3rd percentile with a confirmed early ultrasound EDD, and HC and AC within normal limits, and no evidence of placental insufficiency including normal fetal and maternal dopplers, no history of previous IUGR, PAPP-A (if measured) not low, no maternal history of SLE etc and no past obstetric history of FGR or still birth

Exclusion criteria

• Confirmed aneuploidy or pathogenic copy number variant consistent with fetal anomalies detected by microarray
• Fetuses with confirmed thanatophoric dysplasia, achondroplasia or Apert syndrome on other relevant rapid tests (R23, R24, R25, R306 or R309) are excluded.
• Cases where familial causative variant(s) are known - targeted testing should be performed
• For cases where sonographic findings indicate a specific monogenic disorder, targeted testing should be applied where appropriate
• Where termination of pregnancy has already been decided or when fetal demise has occurred or is imminent then rapid exome sequencing will not be performed. Appropriate testing should be implemented

R21胎儿异常伴可能遗传原因

检测标准

有关 R21 在胎儿全外显子组服务指导文档中概述的更详细指导，请联系您当地的基因组实验室中心。

胎儿超声检测到多发重大结构异常，且多学科审查(包括临床遗传学、三级胎儿医学专家、临床科学家以及适当时相关儿科专家)认为可能为单基因畸形疾病

该指征适用于持续妊娠且遗传诊断可能影响持续妊娠管理的病例，不适用于即将发生胎儿丢失或终止妊娠，或已发生流产的情况

注：该指征用于需要快速/紧急检测时。非紧急检测请使用 R412

临床示例

• 胎儿多发异常、疑似骨骼发育不良(应排除 IUGR)、肾脏大回声增强伴膀胱正常、重大 CNS 异常(排除神经管缺陷)、多发挛缩(排除孤立性双侧马蹄内翻足)。
• 妊娠 11 至 14 周测量的颈项透明层大于 6.5mm 加另一异常(可包括次要发现)，且 array CGH 正常
• 孤立性非免疫性胎儿水肿(在妊娠中晚期常规 18-20 周扫描时或之后检测到)，定义为至少两个腔室(例如皮肤、胸膜、心包或腹水)积液/水肿，且 array CGH 正常
• 持续性颈项透明层(>3.5mm)仅在两个或以上系统存在其他结构异常时方可考虑。
• 次要"非整倍体标志物" - 脉络丛囊肿、回声灶、轻度肾盂扩张、鼻骨短小、长骨位于第 3 百分位等均被排除。
• 轻度脑室扩大只有在两次或以上扫描中后角持续 >11mm 时才应被视为异常。在这种情况下，其单独存在不视为主要 CNS 异常
• 胼胝体异常，部分性或完全性发育不全--单独存在或伴有其他异常
• 近亲夫妇的妊娠，未严格符合上述标准，但认为单基因病可能性大
• 同一夫妇妊娠中特定胎儿异常的复发，未严格符合上述标准，但由于复发认为单基因病可能性大。神经管缺陷除外

以下两项标准可单独作为检测资格标准，或与其他主要异常联合考虑。无多普勒证据的申请将不予处理。

• 小于胎龄儿在以下情况下可考虑符合 R21 资格；所有

测量值<3 rd百分位，并有确认的早期超声估计分娩日期(EDD)扫描，包括腹围(AC)和头围(HC)，且无胎盘功能不全证据，包括胎儿和母体多普勒正常，无既往 FGR 史，PAPP-A(如测量)不低，无母体 SL~~E~~等病史，且无既往 FGR 或死产的产科病史。• 孤立的短长骨可被视为异常，并在以下情况下符合 R21 的条件

情况；所有长骨<3 rd百分位，且有确认的早期超声 EDD，并且 HC 和 AC 在正常范围内，且无胎盘功能不全证据，包括胎儿和母体多普勒正常~~，~~无既往 IUGR 史，PAPP-A(如检测)不低，无母体 SLE 等病史，且无 FGR 或死产的既往产科史

排除标准

• 经微阵列(基因芯片)检测确认的非整倍体或致病性拷贝数变异与胎儿异常一致
• 经其他相关快速检测(R23、R24、R25、R306 或 R309)确认致死性发育不良、软骨发育不全或 Apert 综合征的胎儿除外。
• 已知家族致病变异的情况--应进行靶向检测
• 对于超声所见提示特定单基因病的情况，应酌情应用靶向检测
• 已决定终止妊娠，或已发生胎儿死亡或即将发生时，不进行快速外显子组测序。应实施适当的检测

postnatally using the R27 clinical indication (Paediatric disorders).
• Fetal growth restriction with measurements ≤3rd percentile and evidence of placental insufficiency including abnormal fetal and/or maternal dopplers, low PAPP-A (if measured), past history of FGR or still birth, maternal illness such as SLE cannot be considered as an indication for R21 unless there are other major abnormalities present that indicate a likely genetic aetiology.

Overlapping indications

- R22 Fetus with a likely chromosomal abnormality test should be used instead where findings indicate that a chromosomal cause should be looked for but the additional yield of genomewide sequencing is considered insufficient
- R27 Paediatric disorders should be used for non-urgent testing e.g. where there is imminent fetal loss or termination of pregnancy, or miscarriage has already occurred
- Where findings indicate that there is a likely diagnosis R24 Achondroplasia, R25 Thanatophoric dysplasia or of R23 Apert syndrome, those tests should be used instead
- R14 Acutely unwell children with a likely monogenic disorder should be used for urgent testing in the postnatal setting

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following review in a tertiary fetal medicine unit and after discussion with a Consultant Clinical Geneticist

Referral for testing may be at any point in pregnancy where it will influence clinical management.

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Prenatal

Associated Tests

Please note all the tests below will be undertaken for R21 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R21.1	Fetal anomalies with a likely genetic cause Genomewide Common aneuploidy testing – prenatal	Singleton	Aneuploidy	Genomewide	Genomewide	Common aneuploidy testing
R21.2	Fetal anomalies with a likely genetic cause	Trio	Small variants, CNVs	Panel of genes or loci	Fetal anomalies (478)	Large Panel
R21.3	Fetal anomalies with a likely genetic cause Genomewide Microarray	Singleton	Genomewide	Genomewide	Genomewide	Microarray

产后使用 R27 临床指征(儿科疾病)。

• 胎儿生长受限，测量值<3rd 百分位,并有胎盘功能不全证据,包括胎儿和/或母体多普勒异常、PAPP-A 低(如检测)、既往 FGR 或死产史、母体疾病如 SLE,不能视为 R21 的指征,除非存在其他提示可能遗传病因的主要异常。

重叠指征

• R22 疑似染色体异常的胎儿应改用该检测，当所见提示应寻找染色体病因但认为全基因组范围测序的额外检出率不足时

• R27 儿科疾病应用于非紧急检测，例如存在即将发生的胎儿丢失或终止妊娠，或已发生流产时

• 当所见提示可能诊断为 R24 软骨发育不全、R25 致死性发育不良或 R23 Apert 综合征时，应改用这些检测

• R14 急性不适儿童疑似单基因病应用于紧急检测，在
产后环境

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

经三级胎儿医学单位审查并与顾问临床遗传学家讨论后，转诊检测可在妊娠任何时间点进行，只要其将影响临床管理。申请专科

• 临床遗传学

专科服务组

• 产前

相关检测

请注意，以下所有检测将针对 R21 临床指征申请进行，除非临床表现和/或初始结果提示并非所有检测均必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R21.1	胎儿异常 可能伴有 遗传原因 全基因组范围 常见 非整倍体 检测 – 产前	单人	非整倍体	全基因组范围	全基因组范围	常见非整倍体检测
R21.2	胎儿异常 具有可能的 遗传原因	三人组	小变异，拷贝数变异	基因检测板或基因座	胎儿异常（478）大检测板	
R21.3	胎儿异常 可能伴有 遗传原因 全基因组范围 微阵列（基因芯片）	单人	全基因组范围	全基因组范围	全基因组范围	微阵列（基因芯片）

R412 Fetal anomalies with a likely genetic cause – non urgent

Testing Criteria

Fetus from a demised/non-continued pregnancy, with multiple major structural abnormalities detected on fetal ultrasound or post-mortem examination (by autopsy, imaging, metabolic and/or histological tests) and where multidisciplinary review (clinical genetics, tertiary fetal medicine specialists, clinical scientists and, where appropriate, relevant paediatric specialists) consider a monogenic malformation disorder is likely.

Only for cases where it is not possible to test via R27 (e.g. when there is insufficient DNA for WGS).

Testing should be primarily targeted to those families for which this test may influence future pregnancies.

For more detailed guidance for R412, outlined in the non-urgent fetal exome service guidance documentation, please contact your local Genomic Laboratory Hub.

Overlapping indications

- R27 Paediatric disorders should be used for non-urgent testing e.g. where there is imminent fetal loss or termination of pregnancy, or miscarriage has already occurred
- R14 Acutely unwell children with a likely monogenic disorder, if there is an ongoing unaffected pregnancy and testing is urgent, R14 would be appropriate.
- R21 Fetal anomalies with a likely genetic cause, should be used for ongoing pregnancies where a molecular diagnosis would change clinical management.

Where in Pathway

Following normal aneuploidy and microarray result and exclusion of maternal cell contamination of the DNA sample.

Requesting Specialties

- Clinical Genetics and/or other appropriate specialist referring clinician

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R412.1	Fetal anomalies WES or Large Panel	Trio	Small variants, CNVs	Panel of genes or loci	Fetal anomalies (478)	WES or Large Panel

R412胎儿异常伴可能遗传病因-非紧急

检测标准

已死亡/未继续妊娠的胎儿，经胎儿超声或尸检(通过尸检、影像学、代谢和/或组织学检测)发现多发主要结构异常，且多学科审查(临床遗传学、三级胎儿医学专家、临床科学家以及酌情相关儿科专家)认为单基因畸形疾病可能性大。

仅适用于无法通过 R27 检测的情况(例如 WGS 的 DNA 不足时)。检测应主要针对该检测可能影响未来妊娠的家庭。

有关 R412 的更详细指导，详见非紧急胎儿外显子组服务指导文件，请联系您当地的基因组实验室中心。

重叠指征

- R27 儿科疾病应用于非紧急检测，例如存在即将发生的胎儿丢失或终止妊娠或已发生流产
- R14 急性不适儿童疑似单基因病，如果存在持续未受影响的妊娠与检测属紧急情况，适用R14。
- R21 胎儿异常伴可能遗传病因，应用于持续妊娠，其中分子诊断会改变临床管理。

通路中的位置

在非整倍体和微阵列(基因芯片)结果正常并排除 DNA 样本的母体细胞污染后。

申请专科

- 临床遗传学和/或其他适当的专科转诊临床医生

专科服务组

- 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R412.1	胎儿异常 WES或Large 检测板	三人组	小变异，拷贝数变异	基因组或基因座	胎儿异常（478）	WES或Large 检测板

R251 Non-invasive prenatal sexing

Testing Criteria

Pregnancy requiring non-invasive prenatal sex determination to inform management in pregnancies at risk of severe sex-linked disorders, those affecting one sex in particular or where genitalia are ambiguous

Testing may not be possible in multiple pregnancies. In such cases contact the laboratory for discussion

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Testing performed after 7 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R251.1	Sex determination NIPD	Singleton	Other	Single interval	Other	NIPD

R251无创产前性别鉴定

检测标准

妊娠需要进行无创产前性别鉴定以指导管理，适用于有严重性连锁疾病风险、影响某一性别尤其明显或生殖器模糊的妊娠。多胎妊娠可能无法检测。在此类情况下请联系实验室讨论。检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的情况。

通路中的位置

妊娠7周后经孕龄超声扫描确认进行的检测

申请专科

• 临床遗传学

• 胎儿医学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R251.1	性别鉴定 无创产前检测	单人	其他	单一区间	其他	无创产前检测

R249 NIPD using paternal exclusion testing for very rare conditions where familial variant is known

Testing Criteria

Testing can be offered when paternal exclusion testing can be offered in families at risk of a recessive disorder when parents carry different varints or where the father has an autosomal dominant variant or is known mosaic for a variant. NIPD should only be offered for conditions where invasive testing would otherwise be offered and following discussion with the testing laboratory.

Note: pre-pregnancy work up (R389) is required to enable confirmation that NIPD is possible and to allow timely delivery in pregnancy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Testing should be discussed in advance with the testing laboratory to ensure that necessary samples and validation work has been performed

Testing may not be possible in multiple pregnancies. In such cases contact the laboratory for discussion

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R249.1	Specific target NIPD	Singleton	Other	Single interval	As per tested relative	NIPD

R249NIPD使用父源排除检测用于非常罕见疾病 当家族性变异是已知的

检测标准

当父母携带不同变异，或父亲携带常染色体显性变异或已知为某变异的嵌合体时，对于存在隐性遗传病风险的家系，若可提供父源排除检测，则可提供检测。NIPD 仅应在原本会提供侵入性检测的情况下提供，并须与检测实验室讨论后进行。

注：需要进行孕前评估(R389)，以确认 NIPD 可行，并确保在妊娠期内及时完成。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

应提前与检测实验室讨论检测事宜，以确保已完成必要的样本采集和验证工作。

多胎妊娠可能无法进行检测。此类情况请联系实验室进行讨论。

通路中的位置

妊娠8周后经孕龄超声确认进行的检测

申请专科

• 临床遗传学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R249.1	特定靶标无创产前检测	单人	其他	单一区间	根据受检亲属	无创产前检测

R250 NIPD for congenital adrenal hyperplasia - CYP21A2 haplotype testing

Testing Criteria

1. Pregnancy at risk of 21 hydroxylase deficiency requiring NIPD by haplotype testing following discussion with testing laboratory, AND
2. Parents have had a previous child affected with CAH and have both been confirmed as carriers, AND
3. DNA is available from the parents and the affected child, AND
4. Current pregnancy has been confirmed as XX

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Requests should be discussed in advance with the testing laboratory to ensure that necessary samples and validation work has been performed

Testing may not be possible in multiple pregnancies. In such cases contact the laboratory for discussion

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan. Note pre-pregnancy work up (R389) is required to enable confirmation that NIPD is possible and to allow timely delivery in pregnancy

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R250.1	CYP21A2 NIPD	Singleton	Haplotype testing	Single gene(s)	CYP21A2	NIPD

R250NIPD用于先天性肾上腺增生-CYP21A2单倍型检测

检测标准

1. 妊娠存在 21 羟化酶缺乏症风险，需在与检测实验室讨论后通过单倍型检测进行 NIPD，且
2. 父母曾生育过患 CAH 的子女，且双方均已被确认携带者，且
3. DNA 可从父母和患病孩子处获得，并且
4. 当前妊娠已确认XX

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断能够指导先证者或家系管理的情况。申请应提前与检测实验室讨论，以确保已完成必要的样本采集和验证工作。多胎妊娠可能无法进行检测。此类情况请联系实验室进行讨论。

通路中的位置

在妊娠 8 周后经孕龄扫描确认后进行检测。注：需要进行孕前评估(R389)，以确认 NIPD 可行，并确保在妊娠期内及时完成。

• 临床遗传学
• 胎儿医学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R250.1	CYP21A2 无创产前检;	单人	单倍型检测	单基因	CYP21A2	无创产前检测

R304 NIPD for cystic fibrosis - haplotype testing

Testing Criteria

1. Pregnancy at risk of cystic fibrosis for which NIPD by haplotype testing is required following discussion with testing laboratory AND
2. Each partner carries a confirmed variant and DNA is available from both parents, AND
3. DNA is available from either an affected child/pregnancy OR a confirmed unaffected non-carrier child/pregnancy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Testing may not be possible in multiple pregnancies. In such cases contact the laboratory for discussion

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R304.1	CFTR NIPD - Haplotype Testing	Singleton	Haplotype testing	Single interval	CFTR	NIPD

R304NIPD用于囊性纤维化-单倍型检测

检测标准

1. 妊娠存在囊性纤维化风险，经与检测实验室讨论后需通过单倍型检测进行NIPD，且
2. 双方伴侣均携带已确认的变异，且父母双方的DNA均可获得，且
3. 可从患病儿童/妊娠或已确认未患病非携带者儿童/妊娠获得DNA

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理者。多胎妊娠可能无法进行检测。此类情况请联系实验室讨论

通路中的位置

经孕龄扫描确认在妊娠8周后进行的检测申请专科

专科服务组

- 临床遗传学
- 胎儿医学

专科服务组

- 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R304.1	CFTR 无创产前检测 - 单倍型检测	单人	单倍型检测	单一区间	CFTR	无创产前检测

R305 NIPD for cystic fibrosis - variant testing

Testing Criteria

1. Pregnancy at risk of cystic fibrosis due to known CFTR variant(s) for which NIPD by variant testing is required following discussion with testing laboratory, AND
2. Both parents confirmed to be carriers of a different variant, AND
3. Father is a carrier of one of the following CFTR variants p.(Phe508del), c.489+1G>T, p.(Gly542*), p.(Gly551Asp), p.(Trp1282*) p.(Arg553*), p.(Ile507del), p.(Arg560Thr), p.(Ser549Asn), p.(Ser549Arg)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Testing performed after 9 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics
- Fetal Medicine
- Obstetrics

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R305.1	CFTR NIPD	Singleton	Other, Small variants	Single gene(s)	CFTR	NIPD

R305NIPD用于囊性纤维化-变异检测

检测标准

1. 妊娠因已知CFTR变异存在囊性纤维化风险，经与检测实验室讨论后需通过变异检测进行NIPD，且
2. 父母双方均确认携带不同的变异，且
3. 父亲是以下CFTR变异之一的携带者 p.(Phe508del)、c.489+1G>T、p.(Gly542*)、p.(Gly551Asp)、p.(Trp1282*) p.(Arg553*)、p.(Ile507del)、p.(Arg560Thr)、p.(Ser549Asn)、p.(Ser549Arg) 检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理者。

通路中的位置

妊娠9周后经孕龄超声确认进行的检测

申请专科

• 临床遗传学
• 胎儿医学
• 产科

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R305.1	CFTR 无创产前检测	单人	其他，小型变异	单基因	CFTR	无创产前检测

R306 NIPD for Apert syndrome - variant testing

Testing Criteria

Pregnancy in which NIPD for Apert syndrome is required

Either:

1. Abnormal ultrasound findings suggestive of Apert syndrome with acrocephaly, proptosis AND symmetrical syndactyly, OR
2. At risk pregnancy due to paternal Apert syndrome

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R306.1	FGFR2 NIPD – Apert	Singleton	Small variants	Single gene(s)	FGFR2	NIPD

R306NIPD用于Apert综合征-变异检测

检测标准

本次妊娠需要针对 Apert 综合征进行 NIPD，符合以下任一情况：

1. 超声异常发现提示Apert综合征伴尖头畸形、眼球突出，且对称性并指(趾),OR
2. 因父源 Apert 综合征导致的妊娠风险

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

妊娠8周后经孕龄超声确认进行的检测

申请专科

- 临床遗传学
- 胎儿医学

专科服务组

- 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R306.1	FGFR2 无创产前检测 - 阿佩尔	单人	小变异	单基因	FGFR2	无创产前检测

R307 NIPD for Crouzon syndrome with acanthosis nigricans - variant testing

Testing Criteria

Pregnancy in which NIPD for Crouzon syndrome with acanthosis nigricans is required due to paternal Crouzon syndrome with acanthosis nigricans and the variant is confirmed.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R307.1	FGFR3 NIPD – Crouzon	Singleton	Small variants	Single gene(s)	FGFR3	NIPD

R307NIPD用于Crouzon综合征伴黑棘皮病nigricans-变异检测

检测标准

妊娠需因父源性Crouzon综合征伴黑棘皮病且变异已确认而进行Crouzon综合征伴黑棘皮病的NIPD。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

妊娠8周后经孕龄超声确认进行的检测

申请专科

• 临床遗传学

• 胎儿医学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R307.1	FGFR3 无创产前检测克鲁宗	单人	小变异	单基因	FGFR3	无创产前检测

R308 NIPD for FGFR2-related craniosynostosis syndromes - variant testing

Testing Criteria

Pregnancy in which NIPD for FGFR2-related craniosynostosis is required due to paternal FGFR2-related craniosynostosis with causative variant confirmed.

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R308.1	FGFR2 NIPD - non-Apert FGFR2-related craniosynostosis	Singleton	Small variants	Single gene(s)	FGFR2	NIPD

R308NIPD用于FGFR2相关颅缝早闭综合征-变异检测

检测标准

妊娠需因父源性FGFR2相关颅缝早闭且致病变异已确认而进行FGFR2相关颅缝早闭的NIPD。

通路中的位置

妊娠8周后经孕龄超声确认进行的检测

申请专科

• 临床遗传学

• 胎儿医学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R308.1	FGFR2 NIPD - 非 Apert FGFR2 颅缝早闭	单人	小变异	单基因	FGFR2	无创产前检测

R309 NIPD for FGFR3-related skeletal dysplasias - variant testing

Testing Criteria

Pregnancy in which NIPD for FGFR3-related skeletal dysplasia is required

1. Abnormal ultrasound findings compatible with sonographic diagnosis of achondroplasia or other rare FGFR3-related skeletal dysplasia including Muenke syndrome, hypochondroplasia or hypochondroplasia with acanthosis nigricans:
   a. Femoral length within the normal range at the routine 18-20-week scan, AND
   b. Femur length and all long bones below the 3rd percentile after 25 weeks gestation, AND
   c. Head circumference on or above 95th percentile or above the normal range for gestation at diagnosis and/or frontal bossing present, AND
   d. Fetal and maternal dopplers should be normal
   e. Other features may include polyhydramnios or short fingers

   OR
2. Abnormal ultrasound findings compatible with sonographic diagnosis of thanatophoric dysplasia or severe achondroplasia with developmental delay:
   a. All long bones below the 3rd percentile from early pregnancy, AND
   b. Small chest with short ribs, AND
   c. At least one of: bowed femora, frontal bossing, cloverleaf skull, short fingers

   OR
3. At risk pregnancy due to paternal FGFR3-related skeletal disorder.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Testing may not be possible in multiple pregnancies. In such cases contact the laboratory for discussion.

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R309.1	FGFR3 NIPD - non-Crouzon FGFR3-related skeletal dysplasias	Singleton	Small variants	Single gene(s)	FGFR3	NIPD

R309NIPD用于FGFR3相关骨骼发育不良-变异检测

检测标准

需要进行 FGFR3 相关骨骼发育不良 NIPD 的妊娠

1. 超声异常发现符合软骨发育不全或其他罕见FGFR3相关骨骼发育不良(包括Muenke综合征、软骨发育低下或软骨发育低下伴黑棘皮病)的超声诊断：
   a. 常规18-20周扫描时股骨长度在正常范围内，且
   b. 妊娠25周后股骨长度及所有长骨低于第3百分位，且
   c. 诊断时头围处于或高于第95百分位或高于妊娠正常范围，和/或存在额部隆起，且
   d. 胎儿及母体多普勒检查应正常
   e.其他特征可能包括羊水过多或短指 OR
2. 超声异常发现符合致死性发育不良或严重软骨发育不全伴发育迟缓的超声诊断：
   a.自妊娠早期所有长骨低于第3百分位，且 b.小胸廓伴短肋，且
   c.至少一项：股骨弯曲、额部隆起、三叶草形颅骨、短指或
3. 因父源性 FGFR3 相关骨骼疾病导致的妊娠风险。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理者。多胎妊娠可能无法进行检测。此类情况请联系实验室讨论。

通路中的位置

妊娠8周后经孕龄超声确认进行的检测

申请专科

• 临床遗传学
• 胎儿医学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R309.1	FGFR3 NIPD - 非Crouzon FGFR3相关骨骼发育不良	单人	小变异	单基因	FGFR3	无创产前检测

R310 NIPD for Duchenne and Becker muscular dystrophy - haplotype testing

Testing Criteria

Pregnancy at risk of Duchenne or Becker muscular dystrophy due to known variant for which NIPD by variant testing is required following discussion with testing laboratory

Samples should be available from additional family members to permit testing. Please discuss with the testing laboratory.

Testing may not be possible in multiple pregnancies. In such cases contact the laboratory for discussion

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan, and following a NIPD fetal sexing result that together indicate a single XY fetus

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R310.1	Dystrophin NIPD	Singleton	Haplotype testing	Single gene(s)	Dystrophin	NIPD

R310NIPD用于Duchenne和Becker肌营养不良-单倍型检测

检测标准

妊娠因已知变异存在Duchenne或Becker肌营养不良风险，经与检测实验室讨论后需通过变异检测进行NIPD

应可获得其他家庭成员的样本以进行检测。请与检测实验室讨论。

多胎妊娠可能无法进行检测。此类情况请联系实验室进行讨论。

通路中的位置

经孕龄扫描确认在妊娠8周后进行的检测，且在NIPD胎儿性别鉴定结果共同表明为单一XY胎儿后

申请专科

• 临床遗传学

• 胎儿医学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R310.1	抗肌萎缩蛋白 无创产前	单人	单倍型检测	单基因	抗肌萎缩蛋白	无创产前检测

R311 NIPD for spinal muscular atrophy - variant testing

Testing Criteria

1. Pregnancy at risk of spinal muscular atrophy due to known SMN1 variant(s) for which NIPD by variant testing is required following discussion with testing laboratory, AND
2. Both parents confirmed to be carriers

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Requests should be discussed in advance with the testing laboratory to ensure that necessary samples and validation work has been performed

Testing may not be possible in multiple pregnancies. In such cases contact the laboratory for discussion

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R311.1	SMN1 NIPD	Singleton	Exon level CNVs	Single gene(s)	SMN1	NIPD

R311NIPD用于脊髓性肌萎缩-变异检测

检测标准

1. 妊娠因已知SMN1变异存在脊髓性肌萎缩风险，需通过变异检测进行NIPD需与检测实验室讨论后进行检测，且 2. 父母双方均确认携带者

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断能够指导先证者或家系管理的情况。申请应提前与检测实验室讨论，以确保已完成必要的样本采集和验证工作。多胎妊娠可能无法进行检测。此类情况请联系实验室进行讨论。

通路中的位置

经孕龄扫描确认在妊娠8周后进行的检测申请专科

• 临床遗传学

• 胎儿医学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R311.1	SMN1 无创产前检测	单人	外显子水平拷贝数变异	单基因	SMN1	无创产前检测

R423 NIPD for Retinoblastoma haplotype testing

Testing Criteria

1. Singleton pregnancy at risk of retinoblastoma following discussion with testing laboratory, where either parent or their previous child has a confirmed diagnosis of heritable retinoblastoma by genetic testing (ie maternal, paternal or de novo inheritance) AND
2. For paternal or de novo inheritance - DNA is available from both parents (and affected child where appropriate) OR

   For maternal inheritance testing, DNA must be available from both parents and a previous child (affected or unaffected confirmed genetically)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Requests should be discussed in advance with the testing laboratory to ensure that necessary samples and validation work has been performed.

Testing is not possible in multiple pregnancies.

Where in Pathway

Testing performed after 8 weeks in pregnancy as confirmed by dating scan. N.B. If testing is to be performed using a bespoke NIPD assay, pre-pregnancy work up (R389) is required to enable confirmation that NIPD is possible and to allow timely delivery in pregnancy.

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R423.1	NIPD for Retinoblastoma	Singleton	Haplotype testing	Single gene(s)	RB1	NIPD

R423NIPD用于视网膜母细胞瘤单倍型检测

检测标准

1. 与检测实验室讨论后，存在视网膜母细胞瘤风险的单胎妊娠，其中以下任一情况
   父母或其既往子女经基因检测确诊为遗传性视网膜母细胞瘤(即母源、父源或新发遗传)且

2. 对于父源或新发遗传--需可获得父母双方(及受累子女，如适用)的DNA
   适当)或

   对于母源遗传检测，需可获得父母双方及既往子女(受累或未受累，经基因确认)的DNA

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

申请应提前与检测实验室讨论，以确保已完成必要的样本采集和验证工作。

多胎妊娠无法进行检测。

通路中的位置

经孕龄扫描确认，于妊娠8周后进行检测。注意：若使用定制NIPD检测方法进行检测，需进行孕前准备工作(R389)，以确认NIPD可行并及时在妊娠期完成交付。

申请专科

• 临床遗传学

• 胎儿医学

专科服务组

• 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R423.1	NIPD用于视网膜母细胞瘤	单人	单倍型检测	单基因	RB1	无创产前检测

R389 NIPD - pre-pregnancy test work-up

Testing Criteria

Testing on parental and other family samples to prepare for NIPD in a planned future pregnancy.

Note: this should only be requested in families who qualify for NIPD under the relevant indication and may require further multi-disciplinary or laboratory discussion before approval

Where in Pathway

Prior to the pregnancy in which NIPD is planned

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- NIPD

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R389.1	Specific target NIPD pre-pregnancy work-up	Parents only	Other	Single gene(s)	As per familial diagnosis	NIPD

R389NIPD-孕前检测准备工作

检测标准

对父母及其他家庭成员样本进行检测，为计划中的未来妊娠NIPD做准备。

注意：仅应在符合相关指征下NIPD资格的家庭中申请，且批准前可能需要进一步的多学科或实验室讨论

通路中的位置

在计划进行 NIPD 的妊娠之前

申请专科

• 临床遗传学

专科服务组

• 无创产前检测

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R389.1	特定靶标 NIPD 孕前准备	仅父母	其他	单基因	根据家族性诊断	无创产前检测

R433 Monogenic diabetes, subtype glucokinase - NIPT

Testing Criteria

Pregnancies at 50% risk of maternally inherited monogenic diabetes, subtype glucokinase.

Patients will have undergone genetic testing for monogenic diabetes (indications R141 or R142) and have confirmed genetic diagnosis of GCK monogenic diabetes.

Overlapping indications

- R142 Glucokinase-related fasting hyperglycaemia
- R141 Monogenic diabetes

Where in Pathway

Testing would be performed in pregnancy as confirmed by the first trimester dating scan (after 12 weeks).

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Obstetrics
- Specialist Diabetes Clinics

Specialist Service Group

- Prenatal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R433.1	Monogenic diabetes, subtype glucokinase - NIPT	Singleton	Other	Single interval	GCK	NIPD

R433单基因糖尿病，亚型葡萄糖激酶-NIPT

检测标准

存在50%母源遗传单基因糖尿病(葡萄糖激酶亚型)风险的妊娠。

患者须已接受单基因糖尿病基因检测(指征R141或R142)，并确诊GCK单基因糖尿病。

重叠指征

- R142 葡萄糖激酶相关空腹高血糖
- R141 单基因糖尿病

通路中的位置

检测应在妊娠期进行，经早孕期孕龄扫描确认(12周后)。

申请专科

- 临床遗传学
- 内分泌学
- 产科
- 专科糖尿病门诊

专科服务组

- 产前

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R433.1	单基因糖尿病，葡萄糖激	单人	其他	单一区间	GCK	无创产前检测

Part VII. Gastrohepatology

R168 Non-acute porphyrias

Testing Criteria

Clinical diagnosis of any of the non-acute types of porphyria, including:

- Porphyria cutanea tarda
- Congenital erythropoietic porphyria
- Erythropoietic protoporphyria
- Coproporphyria

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation or after clinical assessment by a highly specialised service

Requesting Specialties

- Dermatology
- Haematology
- Hepatology
- Neurology

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R168.1	Non-acute porphyrias Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Non-acute porphyrias (513)	Small panel

第七部分VII.胃肠肝病学

R168非急性卟啉病

检测标准

任何非急性型卟啉症的临床诊断，包括：

• 迟发性皮肤卟啉症

• 先天性红细胞生成性卟啉症

• 红细胞生成性原卟啉症

• 粪卟啉症

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时或经高度专业化服务临床评估后

申请专科

• 皮肤病学

• 血液学

• 肝脏病学

• 神经科

专科服务组

• 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R168.1	非急性卟啉症 小型检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	非急性卟啉症 (513)	小检测板

R169 Acute intermittent porphyria

Testing Criteria

Clinical features of acute intermittent porphyria (AIP), AND

ALA, PBG, or total porphyrin testing suggests diagnosis of AIP

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation or after clinical assessment by a highly specialised service

Requesting Specialties

- Clinical Genetics
- Dermatology
- Gastroenterology
- Hepatology
- Neurology
- Paediatrics

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R169.1	HMBS Single gene sequencing	Singleton	Small variants	Single gene(s)	HMBS (1207)	Single gene sequencing >=10 amplicons

R169急性间歇性卟啉病

检测标准

急性间歇性卟啉病(AIP)的临床特征，且ALA、PBG或总卟啉检测提示
AIP诊断

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时或经高度专业化服务临床评估后

申请专科

- 临床遗传学
- 皮肤病学
- 胃肠病学
- 肝脏病学
- 神经科
- 儿科

专科服务组

- 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R169.1	HMBS单基因测序	单人	小变异	单基因	HMBS (1207)	单基因测序 >=10扩增子

R170 Variegate porphyria

Testing Criteria

Clinical features of variegate porphyria, AND

ALA, PBG, or total porphyrin testing suggests diagnosis of VP

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Gastroenterology
- Hepatology
- Neurology

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R170.1	PPOX Single gene sequencing	Singleton	Small variants	Single gene(s)	PPOX (1401)	Single gene sequencing >=10 amplicons

R170斑驳卟啉病

检测标准

variegate porphyria的临床特征，以及

ALA、PBG或总卟啉检测提示VP诊断

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 皮肤病学
- 胃肠病学
- 肝脏病学
- 神经科

专科服务组

- 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R170.1	PPOX单基因测序	单人	小变异	单基因	PPOX (1401)	单基因测序 >=10扩增子

R171 Cholestasis

Testing Criteria

Neonatal conjugated hyperbilirubinaemia where multifactorial and infective causes have been excluded, OR

Unexplained cholestasis developing below the age of 18 (It may occasionally be appropriate to test individuals presenting over the 18 under this indication following expert review) OR

Persistence of unexplained cholestasis beyond 3 months or recurrence of otherwise unexplained cholestasis, including those with a suspected precipitating drug OR

Cholestasis of pregnancy onset in the second trimester or serum bile acids >42umol/mL in the third trimester

Testing may occasionally be appropriate outside these criteria following discussion at the national gastrohepatology genomics MDT.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Hepatology
- Metabolic Medicine
- Neonatology
- Paediatrics (on agreement with paediatric hepatologist)

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R171.1	Cholestasis WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Cholestasis (544)	WES or Medium Panel

R171胆汁淤积

检测标准

新生儿结合性高胆红素血症，已排除多因素及感染性病因，或 18岁以下发生的不明原因胆汁淤积(经专家审查后，偶尔可能适合对18岁以上发病者按此指征进行检测)或

不明原因胆汁淤积持续超过3个月或不明原因胆汁淤积复发，包括疑似药物诱发者或

妊娠期胆汁淤积于第二孕期发病或第三孕期血清胆汁酸 >42umol/mL

经全国胃肠肝病基因组MDT讨论后，偶尔可能适合在这些标准之外进行检测。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学
• 肝脏病学
• 代谢医学
• 新生儿科
• 儿科(需经儿科肝病学家同意)

专科服务组

• 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R171.1	胆汁淤积 WES 或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	胆汁淤积 (544)	WES或Medium检测板

R172 Wilson disease

Testing Criteria

High suspicion of Wilson disease, as evidenced by some or all of low caeruloplasmin, high liver copper, high urinary copper, high free copper, Kayser–Fleischer rings

Overlapping indications

- R98 Likely inborn error of metabolism, R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with atypical features in whom a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Hepatology
- Metabolic Medicine
- Neurology
- Psychiatry
- Paediatrics

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R172.1	ATP7B Single gene sequencing	Singleton	Small variants	Single gene(s)	ATP7B (1405)	Single gene sequencing >=10 amplicons

R172Wilson病

检测标准

高度怀疑Wilson病，表现为以下部分或全部：铜蓝蛋白降低、肝铜升高、尿铜升高、游离铜升高、Kayser-Fleischer环

重叠指征

• R98 可能为先天性代谢缺陷，R27 儿科疾病或 R89 超罕见及非典型
单基因疾病检测应用于具有非典型特征且正在考虑更广泛鉴别诊断的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 肝脏病学
• 代谢医学
• 神经科
• 精神病学
• 儿科

专科服务组

• 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R172.1	ATP7B单基因测序	单人	小变异	单基因	ATP7B (1405)	单基因测序 >=10扩增子

R173 Polycystic liver disease

Testing Criteria

Patients with multiple hepatic cysts with no explanation

Overlapping indications

- R193 Cystic renal disease test should be used where patients have both renal and hepatic cysts
- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Hepatology

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R173.1	Polycystic liver disease WES or small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Polycystic liver disease interim (653)	WES or Small Panel

R173多囊性肝病

检测标准

患有多发性肝囊肿且原因不明的患者

重叠指征

• R193 囊性肾病检测应在患者同时具有肾囊肿和肝囊肿时使用

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于

患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 临床遗传学

• 肝脏病学

专科服务组

• 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R173.1	多囊肝疾病 WES 或小panel	单人	小变异，拷贝数变异	基因检测板或基因座	多囊肝病临时 (653)	WES或Small检测板

R175 Pancreatitis

Testing Criteria

1. Clinical diagnosis of recurrent acute pancreatitis (at least 2 attacks), OR
2. Chronic pancreatitis, OR
3. First episode of acute pancreatitis occurring below the age of 18, OR
4. First episode of acute pancreatitis with a first degree relative who has had pancreatitis

In patients where there are no identifiable acquired causes (e.g. gallstones or history of excessive alcohol intake)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Gastroenterology
- Hepatology

Specialist Service Group

- Gastrohepatology

Associated Tests

Please note all the tests below will be undertaken for R175 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R175.1	Pancreatitis Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Pancreatitis (386)	Small panel

R175胰腺炎

检测标准

1. 复发性急性胰腺炎的临床诊断(至少2次发作)，或
2. 慢性胰腺炎，OR
3. 18岁以下首次发生急性胰腺炎，或
4. 首次发作的急性胰腺炎，且有一名一级亲属曾患胰腺炎

患者无可识别的获得性病因(例如胆结石或过量饮酒史)

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 胃肠病学
• 肝脏病学

专科服务组

• 胃肠肝脏病学

相关检测

请注意，对于R175临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R175.1	胰腺炎 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	胰腺炎 (386)	小检测板

R176 Gilbert syndrome

Testing Criteria

Unconjugated hyperbilirubinaemia in the absence of haemolysis, where a molecular diagnosis will contribute to management

Where in Pathway

Test should be requested when a molecular diagnosis will contribute to management

Requesting Specialties

- Clinical Genetics
- Hepatology
- General Practice

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R176.1	UGT1A1 Targeted variant testing	Singleton	Small variants	Single gene(s)	UGT1A1	Targeted variant testing

R176Gilbert综合征

检测标准

无溶血情况下的非结合性高胆红素血症，且分子诊断将有助于管理

通路中的位置

当分子诊断将有助于管理时应申请检测

申请专科

• 临床遗传学
• 肝脏病学
• 全科医疗

专科服务组

• 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R176.1	UGT1A1靶向变异检测	单人	小变异	单基因	UGT1A1	靶向变异检测

R331 Intestinal failure or congenital diarrhoea

Testing Criteria

- Intestinal failure occurring under the age of 18, with dependence on parenteral nutrition over a period of months, with no identifiable underlying cause. **OR**
- Infants presenting with severe and persistent diarrhoea that arises in the neonatal period (first 28 days of life). Severity is defined as requirement for critical care input or parenteral nutrition at any point and persistence for at least 14 days. The disease must be unrelated to surgical short bowel **OR**
- Congenital Short Bowel Syndrome (approx. 50cm in length compared to ~250cm).

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- R15 Primary immunodeficiency test should be used where the presentation is indicative of infantile inflammatory bowel disease

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Gastroenterology
- Neonatology
- Paediatrics

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R331.1	Intestinal failure WES or small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Intestinal failure (514)	WES or Small Panel

R331肠衰竭或先天性腹泻

检测标准

• 18岁之前发生的肠衰竭，依赖肠外营养持续数月，且无可识别的潜在病因。**或**

• 婴儿在新生儿期(出生后最初28天)出现严重且持续的腹泻。严重程度定义为在任何时点需要重症监护支持或肠外营养，且持续至少14天。该疾病必须与手术性短肠无关**或**

• 先天性短肠综合征(长度约50cm，而正常约为250cm)。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

• R15 原发性免疫缺陷检测应在临床表现提示婴儿期时使用炎症性肠病

通路中的位置

申请专科

• 临床遗传学
• 胃肠病学
• 新生儿科
• 儿科

专科服务组

• 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R331.1	肠衰竭 WES或小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	肠衰竭 (514)	WES或Small检测板

R438 Paediatric pseudo-obstruction syndrome

Testing Criteria

The diagnosis of PPOS is confirmed on the presence of at least 2 of the following criteria:
1) Manometric evidence of small intestinal neuromuscular involvement
2) radiological evidence of recurrent and/or persistently dilated loops of small intestine with air fluid levels
3) presence of the genetic, metabolic or other conditions associated with PPOS
4) inability to maintain adequate nutrition and/or growth on oral feeding alone

This test should be used where testing for Hirschsprung disease is required.

Overlapping indications

Patients with intestinal failure should be tested using R331 Intestinal failure or congenital diarrhoea

Where in Pathway

At presentation or following assessment by the highly specialised service.

Requesting Specialties

- Clinical Genetics
- Gastroenterology
- Neonatology
- Paediatrics

Specialist Service Group

- Gastrohepatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R438.1	Paediatric pseudo-obstruction syndrome WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Paediatric pseudo-obstruction syndrome (1217)	WES or Medium Panel

R438儿童假性肠梗阻综合征

检测标准

PPOS的诊断需满足以下标准中至少2项方可确认：
1) 小肠神经肌肉受累的测压证据
2) 影像学证据显示小肠肠袢反复和/或持续扩张并伴有气液平面
3) 存在与PPOS相关的遗传、代谢或其他状况
4) 仅靠口服喂养无法维持充足营养和/或生长

该检测适用于需要进行先天性巨结肠症检测的情况。

重叠指征

肠衰竭患者应使用R331肠衰竭或先天性腹泻进行检测

通路中的位置

就诊时或经高度专业化服务评估后。

申请专科

- 临床遗传学
- 胃肠病学
- 新生儿科
- 儿科

专科服务组

- 胃肠肝脏病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R438.1	儿童假性梗阻综合征WES或中检	单人	小变异，拷贝数变异	基因检测板或基因座	儿童假性肠梗阻综合征 (1217)	WES或Medium检测板

Part VIII. Haematology

R361 Sickle cell, thalassaemia and other haemoglobinopathies trait or carrier testing

Testing Criteria

Individuals who are likely to have or carry a clinically significant haemoglobinopathy trait based on initial protein testing or red cell indices

Overlapping indications

- R93 Sickle cell, thalassaemia and other haemoglobinopathies test should be used in individuals who are likely to be affected with a haemoglobinopathy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following haemoglobin electrophoresis

Requesting Specialties

- Clinical Genetics
- Haematology
- Obstetrics

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R361 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R361.1	HBA1; HBA2; HBG1; HBG2; HBB; HbS	Singleton	Small variants	Small panel	HBA1; HBA2; HBG1; HBG2; HBB (1342)	Small panel
R361.2	HBA1; HBA2; HBG1; HBG2; HBB; HbS MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	HBA1; HBA2; HBG1; HBG2; HBB (1342)	MLPA or equivalent

第VIII部分血液学

R361镰状细胞、地中海贫血及其他血红蛋白病特质或携带者检测

检测标准

根据初始检查，可能患有或携带具有临床意义的血红蛋白病特质的个体
蛋白质检测或红细胞指数

重叠指征

• R93 镰状细胞、地中海贫血及其他血红蛋白病检测应在可能患有血红蛋白病的个体中使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

血红蛋白电泳后

申请专科

• 临床遗传学
• 血液学
• 产科

专科服务组

• 血液学

相关检测

请注意，对于R361临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R361.1	HBA1;HBA2; HBG1；HBG2；HBB；HbS	单人	小变异	小检测板	HBA1；HBA2；HBG1；HBG2；HBB (1342)	小检测板
R361.2	HBA1;HBA2; HBG1；HBG2；HBB；HbS MLPA 或等效	单人	外显子水平拷贝数变异	单基因	HBA1；HBA2；HBG1；HBG2；HBB (1342)	MLPA或等效

R90 Bleeding and platelet disorders

Testing Criteria

Individuals with a bleeding or platelet disorder of likely monogenic aetiology where there are multiple possible causative genes

Overlapping indications

Testing using one of the following targeted indications should be used where appropriate:

- R112 Factor II deficiency
- R115 Factor V deficiency
- R116 Factor VII deficiency
- R117 Factor VIII deficiency
- R118 Factor IX deficiency
- R119 Factor X deficiency
- R120 Factor XI deficiency
- R121 von Willebrand disease
- R122 Factor XIII deficiency
- R123 Combined vitamin K-dependent clotting factor deficiency
- R124 Combined factor V and VIII deficiency

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following consultation with Consultant Haematologist and following relevant functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R90.1	Bleeding and platelet disorders WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Bleeding and platelet disorders (545)	WES or Medium Panel

R90出血及血小板疾病

检测标准

患有可能为单基因病因的出血或血小板疾病且存在多个可能致病基因的个体

重叠指征

在适当情况下应使用以下靶向指征之一进行检测：

• R112 凝血因子II缺乏症
• R115 因子 V 缺乏症
• R116 凝血因子VII缺乏症
• R117 凝血因子VIII缺乏症
• R118 凝血因子IX缺乏症
• R119 凝血因子X缺乏症
• R120 因子XI缺乏症
• R121 血管性血友病
• R122 因子 XIII 缺乏症
• R123 联合维生素K依赖性凝血因子缺乏症
• R124 联合性因子V和VIII缺乏症

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，经血液科顾问医师会诊并完成相关功能性止血检测后

申请专科

• 临床遗传学
• 血液学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R90.1	出血和血小板疾病 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	出血和血小板疾病 (545)	WES或Medium检测板

R93 Sickle cell, thalassaemia and other haemoglobinopathies

Testing Criteria

Clinical features including protein testing or red cell indices indicative of likely thalassaemia or other clinically significant haemoglobinopathy

Overlapping indications

- R92 Rare anaemia test should be used in individuals with atypical features in whom other diagnoses are likely
- R361 Carrier testing for haemoglobinopathy test should be used in individuals who are likely to be carriers of a haemoglobinopathy or haemoglobinopathy trait

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Fetal Medicine
- Haematology
- Obstetrics
- Paediatrics

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R93 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R93.1	HBA1; HBA2; HBG1; HBG2; HBB; HbS MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	HBA1; HBA2; HBG1; HBG2; HBB (1397)	MLPA or equivalent
R93.2	HBA1; HBA2; HBG1; HBG2; HBB; HbS	Singleton	Small variants	Small panel	HBA1; HBA2; HBG1; HBG2; HBB (1397)	Small panel

R93镰状细胞、地中海贫血及其他血红蛋白病

检测标准

临床特征包括蛋白检测或红细胞指数提示可能为地中海贫血或其他具有临床意义的血红蛋白病

重叠指征

- R92 罕见贫血检测应在具有非典型特征且其他诊断可能的个体中使用
  可能的
- R361 血红蛋白病携带者检测应在可能为以下情况的个体中使用
  血红蛋白病或血红蛋白病特质携带者

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 胎儿医学
- 血液学
- 产科
- 儿科

专科服务组

- 血液学

相关检测

请注意，对于R93临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R93.1	HBA1;HBA2; HBG1；HBG2；HBB；HbS MLPA 或等效	单人	外显子水平拷贝数变异	单基因	HBA1；HBA2；HBG1；HBG2； HBB (1397)	MLPA或等效
R93.2	HBA1;HBA2; HBG1；HBG2；HBB；HbS	单人	小变异	小检测板	HBA1；HBA2；HBG1；HBG2； HBB (1397)	小检测板

R372 Newborn screening for sickle cell disease in a transfused baby

Testing Criteria

Newborn screening for sickle cell disease in a baby who has already been transfused

Where in Pathway

As per protocol

Requesting Specialties

- Appropriate specialist referring clinician

Specialist Service Group

- Screening

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R372.1	HbS variant Targeted variant testing	Singleton	Small variants	Single interval	HbS variant	Targeted variant testing

R372新生儿筛查针对镰状细胞病在已输血婴儿

检测标准

已接受输血的婴儿的镰状细胞病新生儿筛查

通路中的位置

按照方案

申请专科

• 适当的专科转诊临床医生

专科服务组

• 筛查

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R372.1	HbS变异 靶向变异检测	单人	小变异	单一区间	HbS变异	靶向变异检测

R95 Iron overload - hereditary haemochromatosis testing

Testing Criteria

Unexplained iron overload (with raised transferrin saturation and/or serum ferritin) suggestive of hereditary haemochromatosis

Overlapping indications

- R96 Iron metabolism disorders - not common HFE variants should be used instead where hereditary haemochromatosis is not the likely diagnosis, or HFE common variants have already been tested for

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics
- Haematology
- Hepatology
- General practice

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R95.1	HFE common variants Targeted variant testing	Singleton	Small variants	Single interval	HFE common variants	Targeted variant testing

R95铁过载-遗传性血色病检测

检测标准

不明原因的铁过载(伴转铁蛋白饱和度升高和/或血清铁蛋白升高)，提示遗传性血色病

重叠指征

• R96 铁代谢障碍 - 非常见 HFE 变异应改为在遗传性
血色病不是可能诊断时使用，或 HFE 常见变异已经检测过。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的患者。

通路中的位置

申请专科

• 心脏病学
• 临床遗传学
• 血液学
• 肝脏病学
• 全科医疗

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R95.1	HFE常见靶向变异变异检测	单人	小变异	单一区间	HFE常见变异	靶向变异检测

R96 Iron metabolism disorders - NOT common HFE variants

Testing Criteria

Iron overload (with raised transferrin saturation and/or serum ferritin) or features of other disorders of iron metabolism in which common HFE variants have been excluded or are unlikely

Overlapping indications

- R95 Iron overload - hereditary haemochromatosis testing should be used where hereditary haemochromatosis due to common HFE variants is likely

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics
- Haematology
- Hepatology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R96.1	Iron metabolism disorders Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Iron metabolism disorders (515)	Small panel

R96铁代谢障碍-非常见HFE变异

检测标准

铁过载(伴转铁蛋白饱和度升高和/或血清铁蛋白升高)或其他铁代谢障碍的特征，其中常见 HFE 变异已被排除或不太可能

重叠指征

• R95 铁过载 - 遗传性血色病检测应在遗传性时使用
由常见 HFE 变异导致的血色病很可能

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 心脏病学
• 临床遗传学
• 血液学
• 肝脏病学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R96.1	铁代谢疾病 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	铁代谢障碍(515) 小panel	

R97 Thrombophilia with a likely monogenic cause

Testing Criteria

- Clinical features indicative of a likely monogenic venous thrombophilia as assessed by a consultant haematologist
- Testing should typically be targeted at those with venous thromboembolic disease at less than 40 years of age, is spontaneous or associated with weak environmental risk factors and which is present in at least one first degree relative
- Testing should only be used where it will impact on clinical management

Where in Pathway

At presentation following consultation with Consultant Haematologist

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R97.1	Thrombophilia WES or small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Thrombophilia (516)	WES or Small Panel

R97血栓形成倾向伴可能单基因病因

检测标准

• 经顾问评估提示可能为单基因静脉血栓形成倾向的临床特征
血液科医生

• 检测通常应针对40岁以下、自发性或与弱环境危险因素相关、且至少一名一级亲属存在的静脉血栓栓塞性疾病患者

• 检测仅应在对临床管理产生影响的情况下使用

通路中的位置

就诊时，经血液科顾问医师会诊后

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R97.1	血栓形成倾向WES或小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	血栓形成倾向 (516)	WES或Small检测板

R112 Factor II deficiency

Testing Criteria

Clinical features characteristic of factor II deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

NOTE: This test is NOT for factor II related thrombophilia. See Thrombophilia with a likely monogenic cause

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R112.1	F2 Single gene sequencing	Singleton	Small variants	Single gene(s)	F2 (1325)	Single gene sequencing >=10 amplicons

R112因子II缺乏症

检测标准

凝血因子II缺乏症的特征性临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

注意：本检测不适用于因子II相关血栓形成倾向。参见可能单基因病因的血栓形成倾向

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R112.1	F2单基因测序	单人	小变异	单基因	F2 (1325)	单基因测序 >=10扩增子

R115 Factor V deficiency

Testing Criteria

Clinical features characteristic of factor V deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

NOTE: This test is NOT for factor V Leiden. See Thrombophilia with a likely monogenic cause

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R115 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R115.1	F5 Single gene sequencing	Singleton	Small variants	Single gene(s)	F5 (1327)	Single gene sequencing >=10 amplicons
R115.2	F5 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	F5 (1327)	MLPA or equivalent

R115因子V缺乏症

检测标准

凝血因子V缺乏症的特征性临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

注意：本检测不适用于因子V Leiden。参见可能单基因病因的血栓形成倾向

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

请注意，对于R115临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R115.1	F5单基因测序	单人	小变异	单基因	F5 (1327)	单基因测序 >=10扩增子
R115.2	F5 MLPA或等效	单人	外显子水平拷贝数变异	单基因	F5 (1327)	MLPA或等效方法

R116 Factor VII deficiency

Testing Criteria

Clinical features characteristic of factor VII deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R116 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R116.1	F7 Single gene sequencing	Singleton	Small variants	Single gene(s)	F7 (1328)	Single gene sequencing >=10 amplicons
R116.2	F7 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	F7 (1328)	MLPA or equivalent

R116因子VII缺乏症

检测标准

凝血因子VII缺乏症的特征性临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

请注意，对于R116临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R116.1	F7单基因测序	单人	小变异	单基因	F7 (1328)	单基因测序 >=10扩增子
R116.2	F7 MLPA或等效	单人	外显子水平拷贝数变异	单基因	F7 (1328)	MLPA或等效方法

R117 Factor VIII deficiency

Testing Criteria

Clinical features characteristic of factor VIII deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R117 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R117.1	F8 Targeted variant testing	Singleton	Small variants	Single gene(s)	F8 (1329)	Targeted variant testing
R117.2	F8 Single gene sequencing	Singleton	Small variants	Single gene(s)	F8 (1329)	Single gene sequencing >=10 amplicons
R117.3	F8 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	F8 (1329)	MLPA or equivalent

R117凝血因子VIII缺乏症

检测标准

凝血因子VIII缺乏症的临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

请注意，对于R117临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R117.1	F8 靶向变异检测	单人	小变异	单基因	F8 (1329)	靶向变异检测
R117.2	F8单基因测序	单人	小变异	单基因	F8 (1329)	单基因测序 >=10扩增子
R117.3	F8 MLPA或等效	单人	外显子水平拷贝数变异	单基因	F8 (1329)	MLPA或等效方法

R118 Factor IX deficiency

Testing Criteria

Clinical features characteristic of factor IX deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R118 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R118.1	F9 Single gene sequencing	Singleton	Small variants	Single gene(s)	F9 (1326)	Single gene sequencing >=10 amplicons
R118.2	F9 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	F9 (1326)	MLPA or equivalent

R118凝血因子IX缺乏症

检测标准

凝血因子IX缺乏症的临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

请注意，以下所有检测均将针对R118临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R118.1	F9单基因测序	单人	小变异	单基因	F9 (1326)	单基因测序 >=10扩增子
R118.2	F9 MLPA或等效	单人	外显子水平拷贝数变异	单基因	F9 (1326)	MLPA或等效

R119 Factor X deficiency

Testing Criteria

Clinical features characteristic of factor X deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R119 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R119.1	F10 Single gene sequencing	Singleton	Small variants	Single gene(s)	F10 (1330)	Single gene sequencing <10 amplicons
R119.2	F10 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	F10 (1330)	MLPA or equivalent

R119凝血因子X缺乏症

检测标准

凝血因子X缺乏症的特征性临床表现

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

请注意，以下所有检测均将针对R119临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R119.1	F10单基因测序	单人	小变异	单基因	F10 (1330)	单基因测序 <10扩增子
R119.2	F10 MLPA或等效	单人	外显子水平拷贝数变异	单基因	F10 (1330)	MLPA或等效

R120 Factor XI deficiency

Testing Criteria

Clinical features characteristic of factor XI deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R120 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R120.1	F11 Single gene sequencing	Singleton	Small variants	Single gene(s)	F11 (1331)	Single gene sequencing >=10 amplicons
R120.2	F11 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	F11 (1331)	MLPA or equivalent

R120因子XI缺乏症

检测标准

因子XI缺乏症的特征性临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

请注意，以下所有检测均将针对R120临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R120.1	F11单基因测序	单人	小变异	单基因	F11 (1331)	单基因测序 >=10扩增子
R120.2	F11 MLPA或等效	单人	外显子水平拷贝数变异	单基因	F11 (1331)	MLPA或等效

R121 von Willebrand disease

Testing Criteria

Clinical features characteristic of von Willebrand disease

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R121 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R121.1	VWF Single gene sequencing	Singleton	Small variants	Single gene(s)	VWF (1404)	Single gene sequencing >=10 amplicons
R121.2	VWF MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	VWF (1404)	MLPA or equivalent

R121血管性血友病病

检测标准

血管性血友病的临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

请注意，以下所有检测均将针对R121临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R121.1	VWF单基因测序	单人	小变异	单基因	VWF (1404)	单基因测序 >=10扩增子
R121.2	VWF MLPA或等效	单人	外显子水平拷贝数变异	单基因	VWF (1404)	MLPA或等效

R122 Factor XIII deficiency

Testing Criteria

Clinical features characteristic of factor XIII deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R122.1	F13A1; F13B	Singleton	Small variants	Small panel	F13A1; F13B (1332)	Small panel

R122凝血因子XIII缺乏症

检测标准

凝血因子XIII缺乏症的特征性临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R122.1	F13A1；F13B	单人	小变异	小检测板	F13A1; F13B (1332)	小检测板

R123 Combined vitamin K-dependent clotting factor deficiency

Testing Criteria

Clinical features characteristic of combined vitamin K-dependent clotting factor deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R123.1	VKORC1; GGCX	Singleton	Small variants	Small panel	VKORC1; GGCX (1316)	Small panel

R123联合维生素K依赖性凝血因子缺乏症

检测标准

联合维生素K依赖性凝血因子缺乏症的临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R123.1	VKORC1; GGCX	单人	小变异	小检测板	VKORC1；GGCX (1316)	小检测板

R124 Combined factor V and VIII deficiency

Testing Criteria

Clinical features characteristic of combined factor V and VIII deficiency

Overlapping indications

- R90 Bleeding and platelet disorders test should be used where features are not typical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following functional haemostasis testing

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R124.1	Combined factor V and VIII deficiency Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Combined factor V and VIII deficiency (517)	Small panel

R124联合因子V和VIII缺乏症

检测标准

遗传性凝血因子V与VIII联合缺乏症的临床特征

重叠指征

• R90 出血和血小板障碍检测应在特征不典型时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

功能性止血检测后就诊时

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R124.1	联合凝血因子V缺乏症和VIII缺乏症小panel	单人	小变异，拷贝数变异	基因检测板或基因座	联合凝血因子V和VIII缺乏症缺乏症 (517)	小检测板

R92 Rare anaemia

Testing Criteria

Rare anaemias of likely monogenic aetiology

Overlapping indications:

R93 Thalassaemia test should be used where the diagnosis is likely to be thalassaemia

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following exclusion of likely acquired causes

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R92 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R92.1	HBA1; HBA2; HBG1; HBG2; HBB; RPL11; RPL35A; RPS17; RPS19; RPS26; RPL5; PKLR MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	HBA1; HBA2; HBG1; HBG2; HBB; RPL11; RPL35A; RPS17; RPS19; RPS26; RPL5; PKLR	MLPA or equivalent
R92.2	HBA1; HBA2; HBG1; HBG2; HBB	Singleton	Small variants	Small panel	HBA1; HBA2; HBG1; HBG2; HBB	Small panel
R92.3	Rare anaemia WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Rare anaemia (518)	WES or Medium Panel

R92罕见贫血

检测标准

可能为单基因病因的罕见贫血

重叠指征：

R93 地中海贫血检测应在诊断可能为地中海贫血时使用

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于

患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

就诊时，在排除可能获得性病因后

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

请注意，以下所有检测均将针对R92临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R92.1	HBA1;HBA2; HBG1；HBG2；HBB；RPL11；RPL35A；RPS17;RPS19; RPS26;RPL5; PKLR MLPA 或等效	单人	外显子水平拷贝数变异	单基因	HBA1；HBA2；HBG1；HBG2；HBB；RPL11；RPL35A；RPS17；RPS19；RPS26；RPL5；PKLR	MLPA或等效
R92.2	HBA1;HBA2; HBG1;HBG2;HBB	单人	小变异	小检测板	HBA1；HBA2；HBG1；HBG2；HBB	小检测板
R92.3	罕见贫血WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	罕见贫血（518）	WES或Medium检测板

R91 Cytopenia - NOT Fanconi anaemia

Testing Criteria

Persistent or recurrent cytopenia or pancytopenia of unknown cause where Fanconi anaemia is unlikely

This includes unexplained isolated aplastic anaemia, thrombocytopenia or neutropenia

Overlapping indications

- R258 Cytopenia – Fanconi breakage testing indicated should be used where exclusion of Fanconi anaemia using chromosome breakage testing is clinically indicated
- R313 Neutropaenia consistent with ELANE variants test should be used in cases of neutropaenia where ELANE variants are plausible and have not been excluded
- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following exclusion of acquired causes including relevant auto-antibodies

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Haematology

Associated Tests

Please note all the tests below will be undertaken for R91 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R91.1	Cytopenia - NOT Fanconi anaemia WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Cytopenia - NOT Fanconi anaemia (519)	WES or Medium Panel
R91.2	RPL11; RPL35A; RPS17; RPS19; RPS26; RPL5; DKC1; TERT; TERC MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	RPL11; RPL35A; RPS17; RPS19; RPS26; RPL5; DKC1; TERT; TERC	MLPA or equivalent

R91血细胞减少-非Fanconi贫血检测标准

不明原因的持续性或复发性血细胞减少或全血细胞减少，且Fanconi贫血可能性不大。包括不明原因的孤立性再生障碍性贫血、血小板减少或中性粒细胞减少

重叠指征

- R258 血细胞减少 - 提示需进行Fanconi断裂检测，应在需要排除Fanconi时使用
  使用染色体断裂试验检测贫血在临床上有指征
- R313 符合ELANE变异的中性粒细胞减少检测，应在中性粒细胞减少病例中使用，当
  ELANE 变异是可能的，且尚未被排除
- R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
  患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

就诊时已排除获得性原因，包括相关自身抗体

申请专科

- 临床遗传学
- 血液学
- 免疫学

专科服务组

- 血液学

相关检测

请注意，以下所有检测均将针对R91临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R91.1	血细胞减少 - 非范可尼贫血 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	血细胞减少 - 非范可尼贫血（519）	WES或Medium检测板
R91.2	RPL11；RPL35A；RPS17；RPS19；RPS26;RPL5; DKC1；TERT；TERC MLF 等效	单人	外显子水平拷贝数变异	单基因	RPL11;RPL35A;RPS17; RPS19；RPS26；RPL5；DKC1； TERT；TERC	MLPA或等效

R258 Cytopenia - Fanconi breakage testing indicated

Testing Criteria

Persistent or recurrent bicytopenia or pancytopenia where exclusion of Fanconi anaemia by chromosome breakage testing is clinically indicated

Overlapping indications

- R91 Cytopenia - NOT Fanconi anaemia test should be used where exclusion of Fanconi anaemia by chromosome breakage testing is not clinically indicated

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R258.1	Fanconi breakage DNA repair defect testing	Singleton	DNA repair	Genomewide	Fanconi breakage	DNA repair defect testing
R258.2	Confirmed Fanconi anaemia or Bloom syndrome WES or Small panel medium	Singleton	Small variants, CNVs	Panel of genes or loci	Confirmed Fanconi anaemia or Bloom syndrome (508)	WES or Small Panel

R258血细胞减少-Fanconi断裂检测有指征

检测标准

持续性或复发性两系血细胞减少或全血细胞减少，且临床上需要通过染色体断裂检测排除Fanconi贫血

重叠指征

• R91 血细胞减少 - 非Fanconi贫血检测，应在需要通过以下方式排除Fanconi贫血时使用
染色体断裂检测无临床指征

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 血液学
• 免疫学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R258.1	范可尼断裂 DNA修复缺陷 检测	单人	DNA修复	全基因组范围	范可尼断裂	DNA修复缺陷 检测
R258.2	确诊范可尼 贫血或Bloom 综合征 WES 或小 panel 中	单人	小变异， 拷贝数变异	基因检测板或 基因座	确诊范可尼贫血或 Bloom综合征(508)	WES或Small 检测板

R259 Nijmegen breakage syndrome

Testing Criteria

1. Molecular findings suggestive of Nijmegen breakage syndrome from genome, exome or other genomic analysis, OR
2. Clinical features characteristic of Nijmegen breakage syndrome

Overlapping indications

- R27 Paediatric disorders, R89 Ultra-rare and atypical monogenic disorders or other broad tests should be used except where clinical features are characteristic of Nijmegen breakage syndrome
- Prenatal diagnosis or cascade testing by chromosome breakage testing will be requested via R240 Diagnostic testing for known familial variant(s)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

N/A

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R259.1	Nijmegen breakage DNA repair defect testing	Singleton	DNA repair	Genomewide	Nijmegen breakage	DNA repair defect testing
R259.2	NBN Single gene sequencing	Singleton	Small variants	Single gene(s)	NBN (1376)	Single gene sequencing >=10 amplicons

R259奈梅亨断裂综合征

检测标准

1. 基因组、外显子组或其他基因组分析提示Nijmegen断裂综合征的分子发现分析，OR
2. Nijmegen 断裂综合征的临床特征

重叠指征

- R27 儿科疾病、R89 超罕见和非典型单基因疾病或其他广泛检测应使用，除非临床特征为Nijmegen断裂综合征的典型表现
- 产前诊断或通过染色体断裂检测进行的级联检测将通过R240申请针对已知家族变异的诊断检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学

专科服务组

- 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R259.1	奈梅亨断裂 DNA修复缺陷检测	单人	DNA修复	全基因组范围	奈梅亨断裂	DNA修复缺陷检测
R259.2	NBN单基因测序	单人	小变异	单基因	NBN（1376）	单基因测序 >=10扩增子

R229 Confirmed Fanconi anaemia or Bloom syndrome - variant testing

Testing Criteria

Confirmed diagnosis of Fanconi anaemia or Bloom syndrome from chromosome breakage analysis requiring variant testing

Overlapping indications

- R91 Cytopenia - NOT Fanconi anaemia test should be used where exclusion of Fanconi anaemia using chromosome breakage testing is clinically indicated
- R260 Fanconi anaemia or Bloom syndrome - chromosome breakage testing test should be used instead where clinical features strongly suggestive of Fanconi anaemia or Bloom syndrome
- In other cases where testing is based on clinical features, R27Paediatric disorders , R89 Ultra-rare and atypical monogenic disorders or other broad genomic tests should typically be used except where clinical features are strongly suggestive of Fanconi anaemia or Bloom syndrome

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following chromosome breakage analysis

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R229.1	Confirmed Fanconi anaemia or Bloom syndrome Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Confirmed Fanconi anaemia or Bloom syndrome (508)	Small panel

R229确诊Fanconi贫血或Bloom综合征-变异检测

检测标准

通过染色体断裂分析确诊Fanconi贫血或Bloom综合征，需要进行变异检测

重叠指征

- R91 血细胞减少 - 非Fanconi贫血检测，应在使用以下方式排除Fanconi贫血时使用染色体断裂检测有临床指征
- R260 Fanconi贫血或Bloom综合征 - 染色体断裂检测应改为使用临床表现高度提示范可尼贫血或Bloom综合征时
- 在其他基于临床特征进行检测的情况下，通常应使用R27儿科疾病、R89 超罕见和非典型单基因疾病或其他广泛基因组检测，除非临床特征强烈提示Fanconi贫血或Bloom综合征

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

进行染色体断裂分析后

申请专科

- 临床遗传学
- 血液学

专科服务组

- 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R229.1	确诊范可尼贫血或Bloom综合征小panel	单人	小变异，拷贝数变异	基因检测板或基因座	确诊范可尼贫血或Bloom综合征(508)	小检测板

R260 Fanconi anaemia or Bloom syndrome - chromosome breakage testing

Testing Criteria

1. Molecular findings suggestive of Fanconi anaemia or Bloom syndrome from genome, exome or other genomic analysis, OR
2. Clinical features strongly suggestive of Fanconi anaemia or Bloom syndrome

Overlapping indications

R258 Cytopenia – Fanconi breakage testing indicated should be used instead where testing is based on haematological clinical features

- In other cases where testing is based on clinical features, R27 Paediatric disorders, R89 Ultra-rare and atypical monogenic disorders or other broad genomic tests should typically be used except where clinical features are strongly suggestive of Fanconi anaemia or Bloom syndrome
- Prenatal diagnosis or cascade testing by chromosome breakage testing will be requested via R240 Diagnostic testing for known familial variant(s)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

N/A

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R260.1	Fanconi breakage DNA repair defect testing	Singleton	DNA repair	Genomewide	Fanconi breakage	DNA repair defect testing

R260Fanconi贫血或Bloom综合征-染色体断裂检测

检测标准

1. 基因组、外显子组或其他基因组分析提示Fanconi贫血或Bloom综合征的分子发现，或

2. 临床特征强烈提示范可尼贫血或Bloom综合征

重叠指征

R258 血细胞减少 - 应改用范可尼断裂试验指征，前提是检测基于血液学临床特征

- 在其他基于临床特征进行检测的情况下，R27 儿科疾病、R89 超罕见和非典型单基因疾病或其他广泛基因组检测，除非临床特征强烈提示Fanconi贫血或Bloom综合征

- 产前诊断或通过染色体断裂检测进行的级联检测将通过R240申请针对已知家族变异的诊断检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 血液学

专科服务组

- 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R260.1	范可尼断裂 DNA修复缺陷检测	单人	DNA修复	全基因组范围	范可尼断裂	DNA修复缺陷检测

R313 Neutropaenia consistent with ELANE variants

Testing Criteria

1. Isolated neutropaenia where ELANE variants are plausible and have not been excluded, AND
2. Family history should NOT indicate autosomal recessive disease, AND
3. Clinical presentation is non-syndromic

Overlapping indications

- R91 Cytopenia – NOT Fanconi anaemia or R258 Cytopenia – Fanconi breakage testing indicated tests should be used where features are atypical of ELANE variants
- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

After exclusion of acquired causes including autoimmune neutropaenia caused by anti-neutrophil antibodies

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R313.1	ELANE Single gene sequencing	Singleton	Small variants	Single gene(s)	ELANE (1372)	Single gene sequencing <10 amplicons

R313中性粒细胞减少症符合ELANE变异

检测标准

1. 孤立性中性粒细胞减少症，且ELANE变异合理且尚未排除，并且
2. 家族史不应提示常染色体隐性遗传病，且
3. 临床表现非综合征性

重叠指征

• R91 血细胞减少 - 非范可尼贫血或R258 血细胞减少 - 范可尼断裂试验指征检测
当特征非典型于ELANE变异时应使用

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

在排除获得性原因后，包括由抗中性粒细胞抗体引起的自身免疫性中性粒细胞减少症

申请专科

• 临床遗传学

• 血液学

• 免疫学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R313.1	ELANE单基因测序	单人	小变异	单基因	ELANE（1372）	单基因测序 <10扩增子

R338 Monitoring for G(M)CSF escape variants

Testing Criteria

Individuals on G(M)CSF requiring detection of escape variants

Where in Pathway

As per relevant clinical protocol

Requesting Specialties

- Haematology
- Immunology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R338.1	CSF3R Single gene sequencing	Singleton	Small variants	Single gene(s)	CSF3R (1358)	Single gene sequencing >=10 amplicons

R338监测G(M)CSF逃逸变异

检测标准

需要检测逃逸变异株的接受G(M) CSF治疗的个体

通路中的位置

按照相关临床方案

申请专科

• 血液学

• 免疫学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R338.1	CSF3R单基因测序	单人	小变异	单基因	CSF3R（1358）	单基因测序 >=10扩增子

R347 Inherited predisposition to acute myeloid leukaemia (AML)

Testing Criteria

Affected individual (proband) where the individual +/- family history meets one of the following criteria. The proband has:

1. AML/MDS AND a pre-existing disorder of platelet function, OR
2. AML/MDS AND ≥1 relative (first / second / third degree relative) with AML/ MDS/ unexplained cytopenia / aplastic anaemia

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M80 Acute myeloid leukaemia should be used for somatic testing

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R347.1	Inherited predisposition to acute myeloid leukaemia AML Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Inherited predisposition to acute myeloid leukaemia (AML) (525)	Small panel

R347遗传性易感性急性髓系白血病(AML)

检测标准

受累个体(先证者)，其个体+/-家族史符合以下标准之一。先证者具有：

1. AML/MDS 且存在既有的血小板功能障碍，或
2. AML/MDS 且≥1名亲属(一级/二级/三级亲属)患有AML/MDS/不明原因血细胞减少 / 再生障碍性贫血

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

• M80 急性髓系白血病应用于体细胞检测

通路中的位置

申请专科

• 临床遗传学
• 血液学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R347.1	遗传性 易感性 急性髓系 白血病 AML 小panel	单人	小变异， 拷贝数变异	基因检测板或 基因座	急性 髓系白血病（AML）（525）	小检测板

R366 Inherited susceptibility to acute lymphoblastoid leukaemia (ALL)

Testing Criteria

Testing of affected individual (proband) where the individual +/- family history meets one of the following criteria

The proband has:

Acute Lymphoblastic Leukaemia (ALL), AND

1. One first / second / third degree relative with ALL, OR
2. Two first / second / third degree relatives with myeloid/lymphoid/platelet disorder

NOTE: All diagnoses must be medically documented

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M91 Acute lymphoblastic leukaemia should be used for somatic testing

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R366.1	PAX5; ETV6	Singleton	Small variants	Small panel	PAX5; ETV6 (1349)	Small panel

R366遗传性易感性至急性淋巴母细胞白血病(ALL)

检测标准

对受累个体(先证者)进行检测，该个体 +/- 家族史符合以下标准之一

先证者具有：

急性淋巴细胞白血病(ALL)，以及

1. 一名一级/二级/三级亲属患有 ALL，或
2. 两名一级/二级/三级亲属患有髓系/淋系/血小板疾病

注意：所有诊断必须有医疗记录

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

• M91 急性淋巴细胞白血病应用于体细胞检测

通路中的位置

申请专科

• 临床遗传学

• 血液学

专科服务组

• 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R366.1	PAX5；ETV6	单人	小变异	小检测板	PAX5；ETV6 (1349)	小检测板

R405 Hereditary Erythrocytosis

Testing Criteria

1. Clinical features of a likely erythrocytosis of monogenic aetiology
2. Exclusion of secondary causes of erythrocytosis and acquired bone marrow disorders such as myeloproliferative neoplasm

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping Indications

- M85 Myeloproliferative neoplasm should be used for somatic testing for exclusion of acquired myeloproliferative neoplasm

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R405.1	Hereditary Erythrocytosis Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Hereditary Erythrocytosis (157)	Small panel

R405遗传性红细胞增多症

检测标准

1. 可能为单基因病因红细胞增多症的临床特征
2. 排除红细胞增多症的继发性原因和获得性骨髓疾病，如骨髓增殖性肿瘤

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

- M85 骨髓增殖性肿瘤应用于体细胞检测以排除获得性骨髓增殖性肿瘤

通路中的位置

申请专科

- 临床遗传学
- 血液学

专科服务组

- 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R405.1	遗传性红细胞增多症小panel	单人	小变异，拷贝数变异	基因检测板或基因座	遗传性红细胞增多症 (157)	小检测板

R406 Thrombocythaemia

Testing Criteria

1. Clinical features of a likely thrombocythaemia of monogenic aetiology

2. Exclusion of secondary causes of thrombocythaemia and acquired bone marrow disorders such as myeloproliferative neoplasm

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping Indications

- M85 Myeloproliferative neoplasm should be used for somatic testing for exclusion of acquired myeloproliferative neoplasm

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Haematology

Specialist Service Group

- Haematology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R406.1	Thrombocythaemia Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Thrombocythaemia (945)	Small panel

R406血小板增多症

检测标准

1. 可能为单基因病因的血小板增多症的临床特征

2. 排除血小板增多症的继发性原因和获得性骨髓疾病，如骨髓增殖性肿瘤

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

- M85 骨髓增殖性肿瘤应用于体细胞检测以排除获得性骨髓增殖性肿瘤

通路中的位置

申请专科

- 临床遗传学
- 血液学

专科服务组

- 血液学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R406.1	血小板增多症小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	血小板增多症 (945)	小检测板

Part IX. Audiology

R65 Aminoglycoside exposure posing risk to hearing

Testing Criteria

Significant exposure to aminoglycosides posing risk of ototoxicity

This indication would be relevant to:

1. individuals with a predisposition to gram negative infections for example due to known respiratory disease (e.g. bronchiectasis, cystic fibrosis) or due to structural or voiding genitourinary tract disorders, OR
2. individuals with hearing loss who have been exposed to aminoglycosides

Overlapping indications

- R67 Monogenic hearing loss should be used in individuals with unexplained hearing loss

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

As appropriate

Requesting Specialties

- Appropriate specialist referring clinician

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R65.1	Aminoglycoside exposure posing risk to hearing	Singleton	Small variants	Single interval	MT-RNR1 m.1555A>G m.1095T>C m.1494C>T	Targeted variant testing

第九部分IX.听力学

R65氨基糖苷类暴露构成风险至听力

检测标准

显著暴露于氨基糖苷类药物，构成耳毒性风险该指征适用于：1. 有革兰阴性菌感染易感性的个体，例如由于已知的呼吸系统

疾病(如支气管扩张、囊性纤维化)或由于结构性或排尿性泌尿生殖道疾病，或

2. 听力损失且曾暴露于氨基糖苷类药物的个体

重叠指征

• R67 单基因听力损失应用于不明原因听力损失的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 适当的专科转诊临床医生

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R65.1	氨基糖苷类暴露构成风险听力	单人	小变异	单区间	MT-RNR1 m.1555A>G m.1095T>C m.1494C>T	靶向变异检测

R67 Monogenic hearing loss

Testing Criteria

Likely or possible monogenic hearing loss

Hearing loss should be confirmed and bilateral

Cases of unilateral hearing loss are accepted IF there are:

(1) additional features suggesting a syndromic hearing loss diagnosis such as Waardenburg / BOR / CHARGE **OR**

(2) a family history of bilateral/unilateral hearing loss consistent with a monogenic cause (for example supported by audiograms).

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At diagnosis, including at confirmation of unexplained hearing loss in the newborn period

Requesting Specialties

- Audiology/Audiovestibular Medicine
- Clinical Genetics
- Ear, Nose and Throat
- Paediatrics

Specialist Service Group

- Audiology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R67.1	Hearing loss WES or large panel	Singleton	Small variants, CNVs	Panel of genes or loci	Hearing loss (126)	WES or Large Panel

R67单基因听力损失

检测标准

可能或疑似单基因听力损失

听力损失应经确认且为双侧

单侧听力损失病例在满足以下条件时可接受：

(1) 提示综合征性听力损失诊断的附加特征，如 Waardenburg / BOR / CHARGE **或**

(2) 符合单基因病因的双侧/单侧听力损失家族史(例如由听力图支持)。

重叠指征

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

在诊断时，包括在新生儿期确认不明原因听力损失时

申请专科

• 听力学/听前庭医学

• 临床遗传学

• 耳鼻喉

• 儿科

专科服务组

• 听力学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R67.1	听力损失 WES 或大检测板	单人	小变异，拷贝数变异	基因检测板或基因座	听力损失 (126)	WES或Large 检测板

Part X. Immunology

R155 Autoimmune Polyendocrine Syndrome

Testing Criteria

Individuals with a clinical diagnosis of autoimmune polyendocrine syndrome

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R155.1	AIRE Single gene sequencing	Singleton	Small variants	Single gene(s)	AIRE (1215)	Single gene sequencing >=10 amplicons

第X部分免疫学

R155自身免疫性多内分泌综合征

检测标准

具有自身免疫性多内分泌综合征临床诊断的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 内分泌学

• 免疫学

专科服务组

• 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R155.1	AIRE单基因测序	单人	小变异	单基因	AIRE (1215)	单基因测序 >=10扩增子

R15 Primary immunodeficiency or monogenic Inflammatory Bowel Disease

Testing Criteria

Suspected primary immunodeficiency diagnosed by a consultant immunologist

Indications include patients with any of the eight International Union of Immunological Societies (IUIS) categories of primary immunodeficiency:

1. Combined immunodeficiency, with or without associated features and abnormal T cell numbers or function. This may include abnormal naïve T cells, TRECs, repertoire, proliferations (e.g. PHA), reversed Cd4/8 ratio or increased gamma delta T cells)
2. Predominantly antibody deficiencies with low or absent vaccine responses
3. Diseases of immune dysregulation including haemophagocytic lymphohistiocytosis (HLH)
4. Congenital defects of phagocyte number, function or both. This should be evidenced by low phagocytic204 numbers and/or abnormal DHR/NBT/phagocytosis/L selectin shedding, Cd11a,b,c or CD18, or abnormal migration or adhesion
5. Defects in intrinsic and innate immunity
6. Autoinflammatory disorders
7. Complement deficiencies with abnormal complement function
8. Testing under these criteria would also include young children with inflammatory bowel disease, defined as: bloody diarrhoea, severe failure to thrive and severe intestinal inflammation with histology consistent with chronic inflammatory intestinal pathology, of onset under 6 years of age

OR

Suspected monogenic IBD diagnosed by a consultant paediatric gastroenterologist, gastroenterologist or immunologist:

1. Infantile onset IBD less than 2 years onset; very early onset IBD (<6years of onset) with severe course (requiring biologics or surgery) or relevant comorbidities and extraintestinal manifestations
2. Testing may occasionally be appropriate outside these criteria following discussion in a specialist MDT, (for example paediatric or young adult IBD with documented severity criteria e.g. relevant family history, comorbidities and extraintestinal manifestations such as infection susceptibility).

Testing Criteria for Semi-Rapid Testing

- Acutely unwell children or adults where primary immunodeficiency or monogenic severe inflammatory bowel disease is considered highly likely to be the primary cause of the phenotype in the patient.

- Cases should meet the standard eligibility criteria for R15, AND

- Where testing will provide an immediate change to treatment or clinical management for the patient.

Notes:

- Cases where the primary clinical indication is NOT primary immunodeficiency or monogenic severe inflammatory bowel disease or where immunodeficiency is part of a more complex presentation should be considered for R14 instead of rapid R15.

- Where a specific immunodeficiency is suspected based on immunological studies (eg X-linked SCID due to IL2RG pathogenic variants) the relevant clinical indication (eg R235 SCID with features of gamma chain deficiency) should be requested instead of rapid R15.

- Please provide relevant immunology data that may aid interpretation of results.

- Clinically urgent cases where the patient is not acutely unwell or where there would be no change to management should be submitted for R15 Primary Immunodeficiency by whole genome sequencing but requested urgently.

- Testing is performed on the proband but please send parental samples if available in order to expedite any further testing that may be required.

R15原发性免疫缺陷或单基因炎症性肠病

检测标准

疑似原发性免疫缺陷，由顾问免疫学家诊断

指征包括具有国际免疫学会联合会(IUIS)八个原发性免疫缺陷类别中任一类的患者：

1. 联合免疫缺陷，伴或不伴相关特征及 T 细胞数量或功能异常。这可能包括异常初始 T 细胞、TRECs、库、增殖(如 PHA)、Cd4/8 比值倒置或 γδ T 细胞增多)
2. 以抗体缺陷为主，伴疫苗应答低下或缺失
3. 免疫失调疾病，包括噬血细胞性淋巴组织细胞增生症(HLH)
4. 吞噬细胞数量、功能或两者兼有的先天性缺陷。这应由低吞噬细胞204数量和/或异常 DHR/NBT/吞噬作用/L 选择素脱落、Cd11a,b,c 或 CD18，或异常迁移或黏附所证实
5. 固有免疫和先天免疫缺陷
6. 自身炎症性疾病
7. 补体功能异常的补体缺陷
8. 在这些标准下进行检测还应包括患有炎症性肠病的幼儿，定义为：血性腹泻、严重生长发育障碍和严重肠道炎症，组织学符合慢性炎症性肠道病理，发病年龄小于 6 岁或

由顾问儿科胃肠病学家、胃肠病学家或免疫学家诊断的疑似单基因 IBD:

1. 婴儿期发病 IBD 小于 2 岁发病；极早发型 IBD(<6 岁发病)伴严重病程(需要生物制剂或手术)或相关合并症和肠外表现
2. 在专科 MDT 讨论后，偶尔可能适合在这些标准之外进行检测(例如具有记录严重程度标准的儿科或青年 IBD，如相关家族史、合并症和肠外表现如感染易感性)。

半快速检测标准

- 急性不适的儿童或成人，其中原发性免疫缺陷或单基因严重炎症性肠病被认为极可能是患者表型的原发原因。

- 病例应符合 R15 的标准资格标准，并且

- 检测将为患者提供治疗或临床管理的即时改变。**备注：**

- 主要临床指征不是原发性免疫缺陷或单基因严重炎症性肠病，或免疫缺陷是更复杂表现的一部分的病例，应考虑 R14 而非快速 R15。

- 若根据免疫学研究怀疑特定免疫缺陷(例如由 IL2RG 致病变异导致的 X 连锁 SCID)，应申请相应的临床指征(例如 R235 具有 γ 链缺陷特征的 SCID)，而非快速 R15。

- 请提供可能有助于结果解读的相关免疫学数据。

- 临床紧急但患者并非急性病重或管理不会改变的病例，应提交 R15 原发性免疫缺陷全基因组测序检测，但需紧急申请。

- 检测在先证者身上进行，但如有父母样本请一并送检，以便加快可能需要的进一步检测。

Overlapping indications

- R16 Severe combined immunodeficiency with adenosine deaminase deficiency test should be used in individuals with ADA deficiency
- R234 Severe combined immunodeficiency with PNP deficiency test should be used in individuals with PNP deficiency
- R235 Severe combined immunodeficiency with gamma chain deficiency test should be used in individuals with low or absent gamma chain or low or absent STAT5 pTyr to IL-2,7, and 15
- R17 Lymphoproliferative syndrome with low or absent SAP expression test should be used in individuals with absent SAP expression
- R232 Lymphoproliferative syndrome with low or absent perforin expression test should be used in individuals with absent perforin expression
- R18 Lymphoproliferative syndrome with low or absent XIAP expression test should be used in individuals with absent XIAP expression
- R19 Autoimmune lymphoproliferative syndrome with defective apoptosis test should be used in individuals with defective Fas-mediated apoptosis, elevated alpha double negative T cells, elevated sFAS or elevated vitamin B12
- R233 Agammaglobulinaemia with low or absent BTK expression test should be used in individuals with absent BTK expression
- R20 Wiskott-Aldrich syndrome test should be used in individuals with a likely diagnosis of WAS
- R204 Amyloidosis with no identifiable cause test should be used in cases with confirmed amyloidosis
- R239 Incontinentia pigmenti testing should be used where there is a high clinical suspicion of this diagnosis. This is because the R15 test is not optimised to detect variants in the IKBKG gene and some diagnoses may be missed.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

N/A

Where in Pathway for Semi-Rapid Testing

At presentation following clinically relevant, rapidly available investigations. All cases must be agreed in advance. Please contact gosh.geneticslab@nhs.net to discuss prior to submitting samples.

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

  Gastroenterology

Requesting Specialties for Semi-Rapid Testing

- Clinical Genetics
- Immunology
- Neonatology

Specialist Service Group

- Immunology

Associated Tests

R15.5 is only for semi urgent testing

重叠指征

• 对于 ADA 缺陷个体，应使用 R16 伴腺苷脱氨酶缺陷的重症联合免疫缺陷检测

• 对于个体，应使用 R234 伴 PNP 缺陷的重症联合免疫缺陷检测
PNP 缺乏症

• 对于 γ 链低或缺如，或对 IL-2、7 和 15 的 STAT5 pTyr 低或缺如的个体，应使用 R235 伴 γ 链缺陷的重症联合免疫缺陷检测

• 对于 SAP 表达缺如的个体，应使用 R17 伴 SAP 表达低或缺如的淋巴增殖综合征检测

• 对于穿孔素表达缺如的个体，应使用 R232 伴穿孔素表达低或缺如的淋巴增殖综合征检测

• 对于 XIAP 表达缺如的个体，应使用 R18 伴 XIAP 表达低或缺如的淋巴增殖综合征检测

• 对于存在 Fas 介导凋亡缺陷、α 双阴性 T 细胞升高、sFAS 升高或维生素 B12 升高的个体，应使用 R19 伴凋亡缺陷的自身免疫性淋巴增殖综合征检测

• 对于 BTK 表达缺如的个体，应使用 R233 伴 BTK 表达低或缺如的无丙种球蛋白血症检测

• 对于可能诊断为 WAS 的个体，应使用 R20 Wiskott-Aldrich 综合征检测

• 对于确诊淀粉样变性的病例，应使用 R204 无可识别病因的淀粉样变性检测

• 当临床高度怀疑色素失禁症诊断时，应使用 R239 色素失禁症检测。这是因为 R15 检测未针对 IKBKG 基因变异检测进行优化，可能漏诊部分诊断。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

半快速检测路径中

在就诊时，于临床相关且可快速获得的检查之后。所有病例必须事先商定。请在提交样本前联系 gosh.geneticslab@nhs.net 进行讨论。

• 临床遗传学

• 血液学

• 免疫学

消化内科

申请专科进行半快速检测

• 临床遗传学

• 免疫学

• 新生儿科

专科服务组

• 免疫学

相关检测

R15.5仅用于半紧急检测

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R15.4	Primary immunodeficiency or monogenic inflammatory bowel disease WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Primary immunodeficiency or monogenic inflammatory bowel disease (398)	WGS
R15.5	Primary immunodeficiency or monogenic inflammatory bowel disease WES	Singleton	Exon level CNVs, Small variants	Panel of genes or loci	Primary immunodeficiency or monogenic inflammatory bowel disease (398)	WES

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R15.4	原发性免疫缺陷或单基因炎症性肠病疾病 WGS(第2阶段	三人组或单人 外显子水平	CNVs，小变异	基因检测板或基因座	原发性免疫缺陷或单基因炎症性肠道疾病 (398)	全基因组测序
R15.5	原发性免疫缺陷或单基因炎症性肠病疾病 WES	单人	外显子水平 CNVs，小变异	基因检测板或基因座	原发性免疫缺陷或单基因炎症性肠道疾病 (398)	全外显子组测序

R413 Autoinflammatory Disorders

Testing Criteria

1. Evidence of recurrent or continuous inflammation (localised or systemic) of otherwise undetermined cause, which fluctuate apparently randomly, either periodically or irregularly **AND**
2. Infectious and autoimmune testing will have been non-diagnostic.

Attacks typically start during childhood but symptoms can also begin during adolescence or even in later adulthood. Main symptom is fever. Other symptoms include serositis (peritonitis, pleuritis and pericarditis), recurrent stroke-like episodes, myalgia, arthralgia and rash, CNS, gastrointestinal and respiratory symptoms.

Overlapping indications

- R15 Primary immunodeficiency or monogenic Inflammatory Bowel Disease

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Immunology
- Rheumatology
- Dermatology
- Gastroenterology
- Paediatrics

Specialist Service Group

- Immunology

Associated Tests

Please note all the tests below will be undertaken for R413 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R413.1	Autoinflammatory Disorders medium panel	Singleton	Small variant detection, CNVs	Panel of genes or loci	Autoinflammatory Disorders (1075)	Medium Panel or WES

R413自身炎症性疾病

检测标准

1. 有证据表明存在原因不明的反复或持续炎症(局部或全身性)
   其波动看似随机，呈周期性或不规则性**且**
2. 感染性和自身免疫性检测结果均为非诊断性。

发作通常始于儿童期，但症状也可始于青春期甚至成年后期。主要症状为发热。其他症状包括浆膜炎(腹膜炎、胸膜炎和心包炎)、反复卒中样发作、肌痛、关节痛和皮疹，以及 CNS、胃肠道和呼吸道症状。

重叠指征

• R15 原发性免疫缺陷或单基因炎症性肠病

通路中的位置

申请专科

• 临床遗传学
• 免疫学
• 风湿病学
• 皮肤病学
• 胃肠病学
• 儿科

专科服务组

• 免疫学

相关检测

请注意，对于 R413 临床指征申请，将进行以下所有检测，除非临床表现和/或初始结果提示所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R413.1	自身炎症性疾病 中等检测组合	单人	小变异检测，拷贝数变异	基因组合或自身炎症性疾病中等基因座	基因组合或WES (1075)	

R16 Severe combined immunodeficiency with adenosine deaminase deficiency

Testing Criteria

T-cell negative/low B-cell negative/low NK-cell negative/low SCID with ADA deficiency

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical and laboratory features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following assessment by a highly specialised service for severe combined immunodeficiency service

Requesting Specialties

- Clinical Genetics
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R16.1	ADA Single gene sequencing	Singleton	Small variants	Single gene(s)	ADA (1388)	Single gene sequencing >=10 amplicons

R16重症联合免疫缺陷伴腺苷脱氨酶缺陷

检测标准

T 细胞阴性/低、B 细胞阴性/低、NK 细胞阴性/低，伴 ADA 缺陷的 SCID

重叠指征

- 当临床和实验室特征不符合时，应使用 R15 原发性免疫缺陷 panel 检测典型基因及更广泛范围的基因均可能为致病原因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

经高度专业化严重联合免疫缺陷服务评估后

申请专科

- 临床遗传学
- 免疫学

专科服务组

- 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R16.1	ADA单基因测序	单人	小变异	单基因	ADA(1388)	单基因测序 >=10扩增子

R235 SCID with features of gamma chain deficiency

Testing Criteria

Males with T-cell negative B-cell positive SCID with low or normal NK-cells with low or absent gamma chain OR low or absent STAT5 pTyr to IL2, IL7, and IL15

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical and laboratory features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following gamma chain and STAT5 tyrosine phosphorylation analysis or following assessment by a highly specialised service for severe combined immunodeficiency service

Requesting Specialties

- Clinical Genetics
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R235.1	IL2RG Single gene sequencing	Singleton	Small variants	Single gene(s)	IL2RG (1386)	Single gene sequencing <10 amplicons

R235SCID伴γ链缺陷特征

检测标准

男性 T 细胞阴性、B 细胞阳性 SCID，伴 NK 细胞低或正常，且 γ 链低或缺如，或对 IL2、IL7 和 IL15 的 STAT5 pTyr 低或缺如

重叠指征

• 当临床和实验室特征不符合时，应使用 R15 原发性免疫缺陷 panel 检测。检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理的病例。

典型基因及更广泛范围的基因均可能为致病原因

通路中的位置

在就诊时，于 γ 链和 STAT5 酪氨酸磷酸化分析后，或经重症联合免疫缺陷高度专业化服务评估后

申请专科

• 临床遗传学

• 免疫学

专科服务组

• 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R235.1	IL2RG单基因测序	单人	小变异	单基因	IL2RG (1386)	单基因测序 <10扩增子

R234 Severe combined immunodeficiency with PNP deficiency

Testing Criteria

T-cell negative/low B-cell negative/low NK-cell negative/low severe combined immunodeficiency with PNP deficiency

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical and laboratory features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following PNP analysis or following assessment by a highly specialised service for severe combined immunodeficiency service

Requesting Specialties

- Clinical Genetics
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R234.1	PNP Single gene sequencing	Singleton	Small variants	Single gene(s)	PNP (1389)	Single gene sequencing <10 amplicons

R234严重联合免疫缺陷伴PNP缺乏

检测标准

T 细胞阴性/低、B 细胞阴性/低、NK 细胞阴性/低，伴 PNP 缺乏的严重联合免疫缺陷

重叠指征

- 当临床和实验室特征不符合时，应使用 R15 原发性免疫缺陷 panel 检测
  典型基因及更广泛范围的基因均可能为致病原因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时、PNP 分析后或经严重联合免疫缺陷高度专业化服务评估后

申请专科

- 临床遗传学
- 免疫学

专科服务组

- 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R234.1	PNP单基因测序	单人	小变异	单基因	PNP(1389)	单基因测序 <10扩增子

R17 Lymphoproliferative syndrome with absent SAP expression

Testing Criteria

Haemophagocytic lymphohistiocytosis (HLH) or other lymphoproliferative disorders affecting males consistent with SAP-related disease and low or absent SAP expression

Typical features may include EBV infection, gammaglobulinaemia or bone marrow aplasia

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical and laboratory features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following SAP expression analysis

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R17.1	SH2D1A Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	SH2D1A (1353)	Single gene sequencing <10 amplicons

R17淋巴增殖性综合征伴SAP表达缺失

检测标准

影响男性、符合 SAP 相关疾病且 SAP 表达低或缺如的噬血细胞性淋巴组织细胞增生症(HLH)或其他淋巴增殖性疾病

典型特征可包括 EBV 感染、丙种球蛋白血症或骨髓再生障碍

重叠指征

- 当临床和实验室特征不符合时，应使用 R15 原发性免疫缺陷 panel 检测
  典型基因及更广泛范围的基因均可能为致病原因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在SAP表达分析之后

申请专科

- 临床遗传学
- 血液学
- 免疫学

专科服务组

- 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R17.1	SH2D1A单基因测序	单人	小变异，拷贝数变异	单基因	SH2D1A (1353)	单基因测序 <10扩增子

R18 Haemophagocytic syndrome with absent XIAP expression

Testing Criteria

Haemophagocytic lymphohistiocytosis (HLH) affecting males consistent with XIAP-related disease and low or absent XIAP expression

Typical features include inflammatory bowel disease or colitis

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical and laboratory features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following XIAP expression analysis

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R18.1	XIAP Single gene sequencing	Singleton	Small variants	Single gene(s), CNVs	XIAP (1344)	Single gene sequencing >=10 amplicons

R18噬血细胞性综合征伴XIAP表达缺失

检测标准

影响男性、符合 XIAP 相关疾病且 XIAP 表达低或缺如的噬血细胞性淋巴组织细胞增生症(HLH)

典型特征包括炎症性肠病或结肠炎

重叠指征

• 当临床和实验室特征不符合时，应使用 R15 原发性免疫缺陷 panel 检测
典型基因及更广泛范围的基因均可能为致病原因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在XIAP表达分析之后

申请专科

• 临床遗传学
• 血液学
• 免疫学

专科服务组

• 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R18.1	XIAP单基因测序	单人	小变异	单基因，拷贝数变异	XIAP(1344)	单基因测序 >=10扩增子

R232 Haemophagocytic syndrome with absent perforin expression

Testing Criteria

Haemophagocytic syndrome with low or absent perforin expression

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical and laboratory features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following perforin expression analysis

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R232.1	PRF1 Single gene sequencing	Singleton	Small variants	Single gene(s)	PRF1 (1343)	Single gene sequencing <10 amplicons

R232噬血细胞性综合征伴穿孔素表达缺失

检测标准

伴低表达或无穿孔素表达的噬血细胞综合征

重叠指征

- 当临床和实验室特征不符合时，应使用 R15 原发性免疫缺陷 panel 检测
  典型基因及更广泛范围的基因均可能为致病原因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在穿孔素表达分析之后

申请专科

- 临床遗传学
- 血液学
- 免疫学

专科服务组

- 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R232.1	PRF1单基因测序	单人	小变异	单基因	PRF1 (1343)	单基因测序 <10扩增子

R19 Autoimmune lymphoproliferative syndrome with defective apoptosis

Testing Criteria

Lymphoproliferative syndrome or other lymphoproliferative disorders consistent with FAS-related disease with:

- abnormal Fas-mediated apoptosis, OR
- elevated alpha beta double negative T cells, OR
- elevated sFAS, OR
- elevated Vitamin B12

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical and laboratory features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following analysis of Fas-mediated apoptosis

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R19.1	FAS Single gene sequencing	Singleton	Small variants	Single gene(s)	FAS (1214)	Single gene sequencing >=10 amplicons

R19自身免疫淋巴增殖性综合征伴缺陷性凋亡

检测标准

淋巴增殖性综合征或其他与 FAS 相关疾病一致的淋巴增殖性疾病，伴：

- Fas 介导的细胞凋亡异常，或
- αβ双阴性T细胞升高，或
- sFAS 升高，或
- 维生素B12升高

重叠指征

- 当临床和实验室特征不符合时，应使用 R15 原发性免疫缺陷 panel 检测典型基因及更广泛范围的基因均可能为致病原因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在对Fas介导的细胞凋亡进行分析后

申请专科

- 临床遗传学
- 血液学
- 免疫学

专科服务组

- 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R19.1	FAS单基因测序	单人	小变异	单基因	FAS（1214）	单基因测序 >=10扩增子

R233 Agammaglobulinaemia with absent BTK expression

Testing Criteria

Clinical features in males suggestive of X-linked agammaglobulinaemia with low or absent BTK expression OR males with absent B cells

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical and laboratory features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following BTK expression analysis

Requesting Specialties

- Clinical Genetics
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R233.1	BTK Single gene sequencing	Singleton	Small variants	Single gene(s)	BTK (1208)	Single gene sequencing >=10 amplicons

R233无丙种球蛋白血症伴BTK表达缺失

检测标准

男性临床特征提示 X 连锁无丙种球蛋白血症伴 BTK 表达降低或缺失，或男性伴 B 细胞缺失

重叠指征

- 当临床和实验室特征不符合时，应使用 R15 原发性免疫缺陷 panel 检测
  典型基因及更广泛范围的基因均可能为致病原因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在BTK表达分析之后

申请专科

- 临床遗传学
- 免疫学

专科服务组

- 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R233.1	BTK单基因测序	单人	小变异	单基因	BTK（1208）	单基因测序 >=10扩增子

R20 Wiskott-Aldrich syndrome

Testing Criteria

Clinical presentation suggestive of Wiskott-Aldrich syndrome (WAS) and limited or absent expression of WASP

The diagnosis should be considered in any male with small platelets

Overlapping indications

- R15 Primary immunodeficiency panel test should be used where clinical features are not typical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, following WASP expression analysis or following assessment by a highly specialised service for severe combined immunodeficiency service

Requesting Specialties

- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R20.1	WAS Single gene sequencing	Singleton	Small variants	Single gene(s)	WAS (1406)	Single gene sequencing >=10 amplicons

R20Wiskott-Aldrich综合征

检测标准

临床表现提示 Wiskott-Aldrich 综合征(WAS)且表达有限或缺失
WASP

任何患有小血小板的男性都应考虑该诊断

重叠指征

• R15 当临床特征不典型时，应使用原发性免疫缺陷 panel 检测，并且
更广泛的基因范围可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在 WASP 表达分析后或经重症联合免疫缺陷高度专业化服务评估后

申请专科

• 临床遗传学

• 血液学

• 免疫学

专科服务组

• 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R20.1	WAS单基因测序	单人	小变异	单基因	WAS（1406）	单基因测序 >=10扩增子

R341 Hereditary angioedema types I and II

Testing Criteria

1. Recurrent non-urticarial angioedema, usually of gradual onset involving the peripheries, gut or larynx, usually of gradual onset and lasting 1-5 days and presenting without a family history, AND
2. Abnormal serum C1INH concentration or function

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following C1INH testing

Requesting Specialties

- Clinical Genetics
- Dermatology
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R341.1	SERPING1 Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	SERPING1 (1345)	Single gene sequencing >=10 amplicons

R341遗传性血管性水肿I型和II

检测标准

1. 反复发作的非荨麻疹性血管性水肿，通常逐渐起病，累及外周、肠道或喉部，通常逐渐起病并持续 1-5 天，且无家族史，AND 2. 血清 C1INH 浓度或功能异常

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 皮肤病学
• 免疫学

专科服务组

• 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R341.1	SERPING1单基因测序	单人	小变异，拷贝数变异	单基因	SERPING1（1345）	单基因测序 >=10扩增子

R368 Hereditary angioedema type III

Testing Criteria

Recurrent non-urticarial angioedema, usually of gradual onset involving the peripheries, gut or larynx, usually of gradual onset and lasting 1-5 days and presenting without a family history, AND

Normal serum C1INH concentration or function

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following complement testing

Requesting Specialties

- Clinical Genetics
- Dermatology
- Immunology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R368.1	F12 hotspot Targeted variant testing	Singleton	Small variants	Single interval	F12 hotspot	Targeted variant testing

R368遗传性血管性水肿III型

检测标准

反复发作的非荨麻疹性血管性水肿，通常逐渐起病，累及外周、肠道或喉部，通常逐渐起病并持续 1-5 天，且无家族史，AND
血清 C1INH 浓度或功能正常

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

以下为补体检测

申请专科

• 临床遗传学
• 皮肤病学
• 免疫学

专科服务组

• 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R368.1	F12热点 靶向变异 检测	单人	小变异	单一区间	F12 热点	靶向变异 检测

R436 Hereditary alpha tryptasaemia

Testing Criteria

Persistently raised mast cell tryptase of 8.0ng/ml or above

Where in Pathway

Clinical suspicion in patients with persistent increased baseline serum tryptase, usually in the context of negative investigation for mastocytosis and other myeloproliferative neoplasms (MPN)

Requesting Specialties

- Immunology
- Haematology
- Paediatrics
- Allergy specialists
- Dermatology

Specialist Service Group

- Immunology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R436.1	Hereditary alpha tryptasaemia	Singleton	Small variants	Single interval	TPSAB1	Targeted variant testing

R436遗传性α类胰蛋白酶血症

检测标准

持续性升高的肥大细胞类胰蛋白酶达8.0ng/ml或以上

通路中的位置

患者基线血清类胰蛋白酶持续升高，临床怀疑，通常是在肥大细胞增多症和其他骨髓增殖性肿瘤(MPN)检查阴性的背景下

申请专科

- 免疫学
- 血液学
- 儿科
- 过敏专科医生
- 皮肤病学

专科服务组

- 免疫学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R436.1	遗传性α类胰蛋白酶血症	单人	小变异	单一区间	TPSAB1	靶向变异检测

Part XI. Inherited cancer

R207 Inherited ovarian cancer (without breast cancer)

Testing Criteria

1. High grade non mucinous epithelial ovarian cancer (EOC) OR serous tubal intraepithelial carcinoma (STIC)at any age

OR

2. Epithelial ovarian cancer (EOC) OR serous tubal intraepithelial carcinoma (STIC) AND

a. ≥1 first degree relative with EOC OR serous tubal intraepithelial carcinoma (STIC) , OR

b. ≥1 second degree relative with EOC OR serous tubal intraepithelial carcinoma (STIC) (intervening relative without ovaries or deceased) OR

c. ≥2 second / third degree relatives with EOC OR serous tubal intraepithelial carcinoma (STIC)

Deceased affected individual (proband) can be tested if:

a. A previously stored constitutional DNA/blood sample is available AND
   i. eligibility criteria 1 OR 2 are reached,
      AND
   ii. No living affected individual is available for genetic testing

OR

b. If no stored constitutional DNA/blood sample is available, but appropriate tissue is available (tumour or normal) AND
   i. Criteria 2 are reached OR pathology-adjusted Manchester score ≥17 or BOADICEA/CanRisk score of ≥15% for affected deceased relative
      AND
   ii. No living affected individual is available for genetic testing

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M2 Ovarian carcinoma should be used for somatic testing

Where in Pathway

At presentation

Requesting Specialties

- Oncology
- Clinical Genetics
- Gynaecology

Specialist Service Group

- Core

第XI部分遗传性癌症

R207遗传性卵巢癌(不伴乳腺癌)

检测标准

1. 任何年龄的高级别非黏液性上皮性卵巢癌(EOC)或浆液性输卵管上皮内癌(STIC)

或

2. 上皮性卵巢癌(EOC)或浆液性输卵管上皮内癌(STIC)AND a.≥1 名一级亲属患 EOC 或浆液性输卵管上皮内癌(STIC),OR b.≥1 名二级亲属患 EOC 或浆液性输卵管上皮内癌(STIC)(中间亲属无卵巢或已故)OR

c. ≥2 名二级/三级亲属患 EOC 或浆液性输卵管上皮内癌(STIC)

已故患病个体(先证者)可在以下情况下进行检测：

a. 已有先前储存的体质性DNA/血液样本可用，且
   i. 达到资格标准 1 或 2，且
   ii. 无在世受累个体可供进行基因检测

或

b. 如无储存的体质性 DNA/血液样本可用，但有合适的组织可用(肿瘤或正常组织)AND
   i. 达到标准 2 OR 经病理校正的 Manchester 评分 ≥17 或 BOADICEA/CanRisk 评分 ≥15%(针对受累已故亲属)AND
   ii. 无在世受累个体可供进行基因检测

注：先证者的癌症以及家族中报告的大多数癌症应已得到确认

在特殊 MDT 讨论并有肿瘤遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

重叠指征

• M2 卵巢癌应用于体细胞检测

通路中的位置

申请专科

• 肿瘤学
• 临床遗传学
• 妇科

专科服务组

• 核心

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R207.1	Inherited ovarian cancer without breast cancer Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Inherited ovarian cancer (without breast cancer) (143)	Small panel

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R207.1	遗传性卵巢癌不伴乳腺癌小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	遗传性卵巢癌（不伴乳腺癌）（143）	小检测板

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R208 Inherited breast cancer and ovarian cancer

Testing Criteria

1. **Living affected individual (proband)** with breast* or high grade ovarian cancer where the individual +/- family history meets one of the criteria. The proband has:
   a. Breast cancer (age <40 years), OR
   b. Bilateral breast cancer (age < 60 years), OR
   c. Triple negative breast cancer (age < 60 years), OR
   d. Assigned male at birth and affected with breast cancer (any age), OR
   e. Breast cancer (age <45 years) and a first degree relative with breast cancer (age <45 years), OR
   f. Combined pathology-adjusted Manchester score ≥15 or single gene pathology adjusted score of ≥10 or BOADICEA/CanRisk score ≥10% OR
   g. Ashkenazi Jewish ancestry and breast cancer at any age
   h. ≥ 1 grandparent from Westray (Orkney) or Whalsay (Shetland) and breast cancer at any age
2. **Living affected individual with pancreatic cancer** AND family history of breast*/high grade ovarian/prostate cancer with a pathology adjusted Manchester score of ≥ 15/CanRisk score of 10%.
3. **Living affected individual with prostate cancer** AND a family history of breast/ovarian/pancreatic cancer with a pathology adjusted Manchester score of ≥ 15/CanRisk score of 10%.
4. **Deceased affected individual** with breast* or high grade ovarian cancer with:
   a. A previously stored constitutional DNA/ blood sample is available, AND i.) Eligibility Criteria 1, 2 or 3 are reached AND ii). No living affected individual is available for genetic testing

   OR

   b. If no stored constitutional DNA/blood sample is available, but appropriate tissue is available (tumour or normal) AND i.) Pathology-adjusted Manchester score ≥17 or BOADICEA/CanRisk score ≥15% , for affected deceased relative AND ii) No living affected individual is available for genetic testing
5. **Living unaffected** individual with:
   a. first degree relative affected by breast* or serous ovarian cancer, AND
   b. Combined pathology-adjusted Manchester score ≥20 or BOADICEA/CanRisk score of ≥20% for affected relative or BOADICEA/CanRisk score of ≥10% for unaffected relative AND
   c. No living affected individual is available for genetic testing, AND
   d. No deceased affected individual with tumour material available for testing

   Note for living unaffected individuals:

   Where more than one family member may be eligible for unaffected testing, the residual probability of a causative pathogenic variant in the family should be considered, taking into account prior normal unaffected tests.

NOTES

- ***Breast cancer definition includes high grade DCIS, LCIS is not included.**
- **The proband's cancer and majority of reported cancers in the family should have been confirmed**
- **The pathology adjusted Manchester score involved incorporation of pathology data for the tested proband alone, i.e. pathology need not be sought for other family members.**
- **Ovarian cancer: Fallopian Tube and Primary Peritoneal cancers can be included**
- **BRCA1/BRCA2 testing should not typically have previously been performed. Exceptions may include, for example, patients who have been tested through the Jewish Community's NHS BRCA-Testing Programme for BRCA1/BRCA2 and not received a molecular diagnosis**
- **Testing of unaffected and deceased individuals can only be offered by Clinical Genetics**

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Overlapping indications

- M2 Ovarian carcinoma should be used for somatic testing
- M3 Breast cancer should be used for somatic testing

R208遗传性乳腺癌和卵巢癌

检测标准

1. **存活受累个体(先证者)**患乳腺癌*或高级别卵巢癌，且该个体 +/- 家族史符合其中一项标准。先证者具有：a.乳腺癌(年龄<40 岁),OR

   b. 双侧乳腺癌(年龄< 60 岁),OR c.三阴性乳腺癌(年龄< 60 岁),OR d.出生时指定为男性且患乳腺癌(任何年龄),OR e.乳腺癌(年龄<45 岁)且有一名一级亲属患乳腺癌(年龄<45 岁),OR f.经病理校正的联合 Manchester 评分 ≥15 或单基因经病理校正评分 ≥10 或 BOADICEA/CanRisk 评分 ≥10% OR

   g.德系犹太人血统且任何年龄患乳腺癌 h.≥ 1 名祖父母来自 Westray(Orkney)或 Whalsay(Shetland)且任何年龄患乳腺癌
2. **存活受累个体患胰腺癌** AND 乳腺癌*/高级别卵巢癌/前列腺癌家族史，经病理校正的 Manchester 评分 ≥ 15/CanRisk 评分 10%。3. **存活受累个体患前列腺癌** AND 乳腺/卵巢/胰腺癌家族史

   病理调整的Manchester评分≥ 15/CanRisk评分10%的癌症。
4. **已故受累个体**患乳腺癌*或高级别卵巢癌，伴：
   a. 有先前储存的体质性 DNA/血液样本可用，AND i.)达到检测资格标准 1、2 或 3 AND ii).无存活受累个体可进行基因检测 OR

   b. 如无储存的体质性DNA/血液样本可用，但有合适的组织可用(肿瘤或正常组织)且 i)经病理校正的Manchester评分≥17或BOADICEA/CanRisk评分≥15%，针对已患病的已故亲属，且 ii)无在世患病个体可供进行基因检测
5. **无患病表现**的个体，具备：
   a. 一级亲属患有乳腺癌*或浆液性卵巢癌，且
   b. 经病理校正的合并Manchester评分≥20或患病亲属的BOADICEA/CanRisk评分≥20%或未患病亲属的BOADICEA/CanRisk评分≥10%，且
   c. 无在世受累个体可供进行基因检测，且

   d.无已故患病个体留有可供检测的肿瘤材料对在世未患病个体的说明：

   当多名家庭成员可能符合未患病检测资格时，应考虑家族中致病性变异残余概率，并计入既往未患病检测正常的结果。

备注

- ***乳腺癌定义包括高级别DCIS，不包括LCIS。**
- **先证者的癌症及家族中报告的大多数癌症应已得到确认**
- **经病理校正的Manchester评分涉及纳入受检者的病理数据仅先证者，即无需寻求其他家庭成员的病理资料。**
- **卵巢癌：可包括输卵管癌和原发性腹膜癌**
- **通常不应既往已进行过BRCA1/BRCA2检测。例外情况可能包括，例如，已通过犹太社区NHS BRCA检测项目接受BRCA1/BRCA2检测且未获得分子诊断的患者**
- **未患病个体和已故个体的检测只能由临床遗传学部门提供**

在有癌症遗传学家出席的专科MDT讨论后，偶尔可能适合在这些标准之外进行基因检测

重叠指征

- M2 卵巢癌应用于体细胞检测
- M3 乳腺癌检测应用于体细胞检测

- R444 NICE approved PARP inhibitor treatment

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Oncology
- Clinical Genetics
- Surgery

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R208.1	Inherited breast and ovarian cancer	Singleton	Small variants, CNVs	Small panel of genes	Inherited breast and ovarian cancer (635)	Small panel

• R444 NICE 批准的 PARP 抑制剂治疗

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 肿瘤学
• 临床遗传学
• 手术

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R208.1	遗传性乳腺和卵巢癌	单人	小变异，拷贝数变异	小检测板基因	遗传性乳腺和卵巢癌（635）	小检测板

R210 Inherited MMR deficiency (Lynch syndrome)

Testing Criteria

All new diagnoses of colorectal and endometrial cancer should have tumour MSI / IHC as outlined in the cancer test directory and the Lynch syndrome handbook for Alliances in order to identify dMMR tumours and additional testing that suggests Lynch Syndrome. This may include BRAF testing in MLH1 deficient colorectal cancers and somatic MLH1 hypermethylation testing in BRAF negative colorectal cancers and all MLH1 deficient uterine cancers. Somatic MLH1 hypermethylation testing is included on the Cancer Test Directory under M1.5.

1. **Clinical Criteria for germline testing in an affected individual**
   The proband has a dMMR tumour where results of additional testing suggest Lynch syndrome. This may include BRAF testing in MLH1 deficient colorectal cancers and somatic MLH1 hypermethylation testing in BRAF negative colorectal cancers and all MLH1 deficient uterine cancers
   a. The affected proband comes from a modified Amsterdam criteria positive family irrespective of the dMMR status of the tumour
   b. Personal or family history suggestive of Constitutional Mismatch Repair Deficiency (CMMRD) with Wimmer score =>3
   c. Deceased affected individual meets criteria and a previously stored constitutional blood/DNA sample is available.

2. **Clinical criteria for MSI /IHC testing on a stored tumour sample prior to germline testing**
   a. Personal/family history of colorectal cancers reaching Modified Amsterdam Criteria (≥ 3 cases of Lynch related cancer over ≥2 generations with ≥1 case diagnosed <50 years) OR
   b. Any lynch-related cancer* <50 years (excluding isolated pancreas, prostate or gastric cancers)
   c. Two Lynch-related cancers (any age, one is colorectal or endometrial), OR
   d. Lynch-related cancer and ≥ 1 first degree relative has Lynch-related cancer (both occurred ≤60 years, one is colorectal or endometrial), OR
   e. Lynch-related cancer and ≥ 2 relatives (first / second / third degree relatives) have Lynch-related cancer (all occurring ≤75years, one is colorectal or endometrial), OR
   f. Lynch-related cancer and ≥ 3 relatives (first / second / third degree relatives) have Lynch-related cancer (occurring any age, one is colorectal or endometrial)

*Lynch-related cancers comprise: Colorectal cancer, Endometrial cancer, Epithelial ovarian cancer, Urothelial cancers, Transitional cell cancer of renal pelvis, cholangiocarcinoma, Small bowel and upper gastrointestinal cancers, Glioblastoma, endocervical cancer, at least two sebaceous adenomas, one or more sebaceous carcinoma, prostate, gastric and pancreas. A single sebaceous adenoma does not constitute a Lynch-related cancer.

3. **Clinical Criteria for somatic (tumour) Lynch syndrome panel testing**
   a. Proband has colorectal or endometrial cancer with a dMMR tumour with normal BRAF and somatic MLH1 hypermethylation analysis AND germline testing did not reveal a pathogenic variant OR personal/family pattern of disease whereby demonstration of acquired MMR variants (and therefore exclusion of constitutional MMR abnormality) enables downscaling of surveillance
   b. Deceased affected individual with colorectal or endometrial cancer ≤60 years AND tumour featuring high/intermediate MSI or loss of staining of MMR protein(s) on IHC, AND one first degree relative with Lynch-related cancer ≤60 AND no living affected individual is available for genetic testing.

4. **Clinical Criteria for germline testing in an unaffected individual**
   a. First degree relative affected with Lynch-related cancer, AND
   b. Family history of colorectal cancer/Lynch-related cancers reaches Amsterdam Criteria (≥3 cases over ≥2 generations with ≥1 case affected <50 years) AND
   c. Tumour sample analysis from affected family member has been attempted and is not possible, failed, indeterminate or indicates MMR deficiency (via IHC or MSI), AND
   d. Somatic sequencing is not possible, or failed, AND
   e. No living affected individual is available for genetic testing

5. **Criteria for germline MLH1 promoter methylation**
   a. Families where MLH1 promotor methylation has been identified in tumour tissue in >1 affected individual with colorectal cancer ≤ 60

R210遗传性MMR缺陷(Lynch综合征)

检测标准

所有新诊断的结直肠癌和子宫内膜癌均应按照癌症检测目录和联盟 Lynch 综合征手册的规定进行肿瘤 MSI / IHC 检测，以识别 dMMR 肿瘤以及提示 Lynch 综合征的其他检测。这可能包括对 MLH1 缺陷型结直肠癌进行 BRAF 检测，以及对 BRAF 阴性结直肠癌和所有 MLH1 缺陷型子宫癌进行体细胞 MLH1 高甲基化检测。体细胞 MLH1 高甲基化检测已纳入癌症检测目录 M1.5 项下。

1. **受累个体的胚系检测临床标准**
   先证者患有dMMR肿瘤，额外检测结果提示Lynch综合征。这可能包括对MLH1缺陷型结直肠癌进行BRAF检测，以及对BRAF阴性结直肠癌和所有MLH1缺陷型子宫癌进行体细胞MLH1高甲基化检测
   a. 患病先证者来自改良Amsterdam标准阳性家族，无论肿瘤dMMR状态如何
   b. 个人史或家族史提示体质性错配修复缺陷(CMMRD),Wimmer评分=>3
   c. 已故患病个体符合标准，且有先前储存的体质性血液/DNA样本可用。

2. **在胚系检测前对储存肿瘤样本进行MSI/IHC检测的临床标准**
   a. 个人/家族史有结直肠癌达到改良Amsterdam标准(≥2代中≥3例Lynch相关癌症，其中≥1例诊断<50岁)或
   b. 任何Lynch相关癌症*<50岁(不包括孤立性胰腺癌、前列腺癌或胃癌)
   c. 两种Lynch相关癌症(任何年龄，其一为结直肠癌或子宫内膜癌)，或
   d. Lynch相关癌症且≥1名一级亲属患有Lynch相关癌症(两者均发生≤60岁，其中之一为结直肠癌或子宫内膜癌)，或
   e. Lynch相关癌症且≥2名亲属(一级/二级/三级亲属)患有Lynch相关癌症(均发生≤75岁，其中之一为结直肠癌或子宫内膜癌)，或
   f. Lynch相关癌症且≥3名亲属(一级/二级/三级亲属)患有Lynch相关癌症(发生于任何年龄，其中之一为结直肠癌或子宫内膜癌)

*Lynch相关癌症包括：结直肠癌、子宫内膜癌、上皮性卵巢癌、尿路上皮癌、肾盂移行细胞癌、胆管癌、小肠和上消化道癌症、胶质母细胞瘤、宫颈内膜癌、至少两个皮脂腺瘤、一个或多个皮脂腺癌、前列腺癌、胃癌和胰腺癌。单个皮脂腺瘤不构成Lynch相关癌症。

3. **体细胞(肿瘤)Lynch综合征panel检测的临床标准**
   a. 先证者患有结直肠癌或子宫内膜癌，肿瘤为dMMR且BRAF正常及体细胞MLH1高甲基化分析正常，且胚系检测未发现致病性变异，或个人/家族疾病模式表明证实获得性MMR变异(从而排除体质性MMR异常)可使监测降级
   b. 已故患病个体患有结直肠癌或子宫内膜癌≤60岁，且肿瘤表现为高/中度MSI或IHC显示MMR蛋白染色缺失，且一名一级亲属患有Lynch相关癌症≤60岁，且无在世患病个体可供进行基因检测。

4. **未患病个体进行胚系检测的临床标准**
   a. 一级亲属患有Lynch相关癌症，且
   b. 结直肠癌/Lynch相关癌症家族史达到Amsterdam标准(≥2代中≥3例，其中≥1例患病<50岁)且
   c. 已尝试对患病家庭成员的肿瘤样本进行分析但无法进行、失败、结果不确定或提示MMR缺陷(通过IHC或MSI)，且
   d. 体细胞测序不可行或失败，且
   e. 无在世受累个体可供进行基因检测

5. **胚系MLH1启动子甲基化的标准**
   a. 在超过1名结直肠癌≤60岁的受累个体中，肿瘤组织已发现MLH1启动子甲基化的家族

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

Testing of unaffected individuals can only be carried out by Clinical Genetics Services

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M1.9 Multi-target NGS panel - small variant (MLH1, MSH2, MSH6, PMS2, POLE, POLD1) (M1 Colorectal carcinoma) should be used for somatic testing

Where in Pathway

At presentation following tumour studies (IHC/MSI)

Requesting Specialties

- Clinical Genetics
- Oncology
- Surgery*
- Gastroenterology
- Histopathology
- Dermatology

* Surgery to cover colorectal and gynecological surgeons

Specialist Service Group

- Core

Associated Tests

Please note that not all the associated tests will be undertaken in every case. The clinical presentation will indicate the tests that are necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R210.2	Inherited MMR deficiency Lynch syndrome Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Inherited MMR deficiency (Lynch syndrome) (503)	Small panel
R210.4	Germline MLH1 promotor methylation	Singleton	Methylation	Single gene(s)	MLH1	Methylation testing
R210.6	Inherited MMR deficiency (Lynch syndrome)	Singleton	Exon level CNVs	PMS2	PMS2	MLPA or equivalent

注：先证者的癌症以及家族中报告的大多数癌症应已得到确认

未受累个体的检测只能由临床遗传学服务部门进行

在有癌症遗传学家出席的专科MDT讨论后，偶尔可能适合在这些标准之外进行基因检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

• M1.9 多靶点NGS panel - 小变异(MLH1、MSH2、MSH6、PMS2、POLE、POLD1)(M1 结直肠癌)应使用于体细胞检测

通路中的位置

就诊时经肿瘤相关检测(IHC/MSI)后

申请专科

• 临床遗传学
• 肿瘤学
• 手术*
• 胃肠病学
• 组织病理学
• 皮肤病学

* 结直肠外科和妇科外科医生的手术覆盖

专科服务组

• 核心

相关检测

请注意，并非所有相关检测都会在每个病例中进行。临床表现将指示必要的检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R210.2	遗传性MMR缺陷Lynch综合征 小检测组合	单人	小检测板变异，拷贝数变异	基因组或基因座	遗传性MMR缺陷(Lynch综合征) (503)	小检测板
R210.4	胚系MLH1启动子甲基化	单人	甲基化	单基因	MLH1	甲基化检测
R210.6	遗传性MMR缺陷（Lynch综合征）	单人	外显子水平拷贝数变异	PMS2	PMS2	MLPA或等效方法

R211 Inherited polyposis and early onset colorectal cancer - germline test

Testing Criteria

Living affected individual (proband) where the individual +/- family history meets **one** of the criteria. The proband has:

1. Any colorectal cancer OR endometrial cancer diagnosis under 40 years
2. Any small bowel cancer diagnosis under 40 years
3. Proband has endometrial or colorectal cancer (CRC) with ≥2 siblings with CRC/EC, where at least 1 diagnosed <50
3. ≥5 adenomatous polyps and colorectal cancer, OR
4. ≥5 adenomatous polyps (age <40 years), OR
5. ≥10 adenomatous polyps (age <60 years, OR
6. ≥20 adenomatous polyps (age ≥ 60 years), OR
7. ≥5 adenomatous polyps (age <60 years) and first degree relative with ≥5 adenomatous polyps or CRC (age <60 years), OR
8. A clinical diagnosis of serrated polyposis syndrome* IF:
   a. patient aged < 50 OR
   b. family history of ≥1 affected FDR with SPS OR
   c. evidence of dysplasia within any polyp

*Clinical diagnosis of Serrated Polyposis Syndrome:

a. Five or more serrated lesions/polyps proximal to the rectum all being at least 5 mm in size with two or more being at least 10mm in size,
b. More than 20 serrated lesions/polyps of any size distributed through the large bowel with at least five being proximal to the rectum.

9. Hamartomatous polyposis syndromes:
   a. ≥ 5 hamartomatous polyps of the colorectum, OR
   b. ≥ 2 hamartomatous polyps throughout the GI tract, OR
   c. ≥ 1 hamartomatous polyp and a first / second degree relative has hamartomatous polyp.

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND
(ii) a previously stored constitutional blood/DNA sample is available, AND
(iii) no living affected individual is available for genetic testing, AND
(iv) after discussion at specialist cancer genetics MDT

NOTE: The majority of polyps are histologically confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Overlapping indications

- Inherited polyposis – somatic test should be used if no living affected individual is available for germline testing, no germline DNA sample has been stored from a deceased affected individual, and a molecular diagnosis is required to advise living relatives
- M1 Colorectal carcinoma should be used for somatic testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

R211遗传性息肉病和早发性结直肠癌-胚系检测

检测标准

存活的受累个体(先证者)，其中该个体+/-家族史符合**其中一项**标准。先证者具有：

1. 任何40岁以下的结直肠癌或子宫内膜癌诊断
2. 40岁以下任何小肠癌诊断
3. 先证者患有子宫内膜癌或结直肠癌(CRC)，且有≥2个兄弟姐妹患有CRC/EC，其中至少1人在<50岁确诊

3. ≥5个腺瘤性息肉和结直肠癌，或
4. ≥5个腺瘤性息肉(年龄<40岁),或
5. ≥10个腺瘤性息肉(年龄<60岁,或
6. ≥20个腺瘤性息肉(年龄≥60岁)，或
7. ≥5个腺瘤性息肉(年龄<60岁)且一级亲属有≥5个腺瘤性息肉或CRC(年龄<60岁),或

8. 锯齿状息肉病综合征的临床诊断*，如果：
   a. 患者年龄< 50 或
   b. ≥1名患SPS的一级亲属家族史或
   c. 任何息肉内存在异型增生的证据

诊断为锯齿状息肉病综合征：a.五个或更多锯齿状病变/息肉位于直肠近端，所有病变至少5 mm大小，其中两个或更多至少10mm大小，

*

b. 超过20个任何大小的锯齿状病变/息肉分布于大肠，其中至少五个位于直肠近端。

9. 错构瘤性息肉病综合征：
   a. 结直肠≥5个错构瘤性息肉，或
   b. ≥ 2 个错构瘤性息肉遍布胃肠道，或
   c. ≥ 1个错构瘤性息肉且一级/二级亲属有错构瘤性息肉。

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA样本可用，且(iii)没有存活的受累个体可用于基因检测，且(iv)经专科癌症遗传学MDT讨论后

注：大多数息肉经组织学确诊

在有癌症遗传学家出席的专科MDT讨论后，偶尔可能适合在这些标准之外进行基因检测

重叠指征

• 遗传性息肉病 - 如果没有存活的受累个体可用于胚系检测，应使用体细胞检测检测，没有从已故受累个体储存的胚系DNA样本，且需要分子诊断以指导存活亲属

• M1 结直肠癌应用于体细胞检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

Requesting Specialties

- Clinical Genetics
- Gastroenterology
- Gynaecology
- Surgery*

*Surgery to cover colorectal surgeons

Specialist Service Group

- Core

Associated Tests

Please note all the tests below will be undertaken for R211 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R211.1	Inherited polyposis and early onset colorectal cancer - germline testing	Singleton	Small variants, CNVs	Panel of genes or loci	Inherited polyposis (504)	Small panel
R211.3	Inherited polyposis and early onset colorectal cancer - germline testing	Singleton	Exon level CNVs	PMS2	PMS2	MLPA or equivalent

申请专科

- 临床遗传学
- 胃肠病学
- 妇科
- 手术*

* 结直肠外科医师覆盖手术

专科服务组

- 核心

相关检测

请注意，对于R211临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R211.1	遗传性息肉病以及早发性结直肠癌--胚系检测	单人	小变异，拷贝数变异	基因检测板或基因座	遗传性息肉病（504）	小检测板
R211.3	遗传性息肉病及早发性结直肠癌--胚系检测	单人	外显子水平拷贝数变异	PMS2	PMS2	MLPA或等效

R414 APC Associated Polyposis

Testing Criteria

Testing in children / young adults who may be too young to have developed bowel polyps. To be done prior to colonoscopy, on the basis of one or more of the following APC-associated findings:

1. Multifocal or bilateral CHRPE as assessed by experienced Ophthalmologist, OR
2. Aggressive fibromatosis/Desmoid tumour (CTNNB1 WT where testing performed) OR
3. Cribriform-morular variant of papillary thyroid cancer OR
4. Hepatoblastoma OR
5. Multiple osteomas of skull and mandible or multiple dental abnormalities (unerupted teeth, supernumerary teeth with dentigerous cysts or odontomas) in children/young adults
6. Affected individual of any age with gastric polyposis meeting GAPPs criteria* OR
7. Classic type medulloblastoma
8. Patient with pilomatrixoma(s) without syndromic features consistent with alternative diagnosis (e.g. Rubenstein Taybi/Myotonic Dystrophy/Kabuki Syndromes etc) AND one of the following:

a. ≥6 pilomatrixomas at any age OR
b. ≥2 pilomatrixoma <20 OR
c. Single pilomatrixoma in an individual with ≥ 1 other APC-associated feature OR
d. Pilomatrixoma with features of an epidermoid cyst

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

*Footnote: Diagnostic criteria of GAPPS (Worthley et al. Gut. 2012 May;61(5):774-9). GAPPs criteria apply to all individuals and not just children or young adults.

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Overlapping indications

R211 for individuals with polyposis who should proceed to full polyposis panel

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Surgery
- Dermatology
- Oncology*

*including paediatrics

Specialist Service Group

- Core

R414APC相关息肉病

检测标准

对可能太年轻而尚未发生肠息肉的儿童/年轻成人进行检测。基于以下一项或多项APC相关发现，在结肠镜检查之前进行：

1. 由经验丰富的眼科医生评估的多灶性或双侧CHRPE，或
2. 侵袭性纤维瘤病/硬纤维瘤(如进行检测，则为 CTNNB1 WT)或
3. 筛状-桑葚样变异型甲状腺乳头状癌或
4. 肝母细胞瘤或
5. 儿童/年轻成人中颅骨和下颌骨多发性骨瘤或多发性牙齿异常(未萌出牙、含牙囊肿或牙瘤的额外牙)
6. 任何年龄的胃息肉病且符合 GAPPs 标准的受累个体* 或
7. 经典型髓母细胞瘤
8. 患者有毛母质瘤而无符合替代诊断(如Rubenstein Taybi/强直性肌营养不良/Kabuki综合征等)的综合征特征，且具有以下之一：a.任何年龄≥6个毛母质瘤或<20岁≥2个毛母质瘤或具有≥ 1个其他APC相关特征的个体中单个毛母质瘤或具有表皮样囊肿特征的毛母质瘤
b.
c.
d.

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

*脚注：GAPPS的诊断标准(Worthley等。Gut。2012年5月；61(5):774-9)。GAPPs标准适用于所有个体，而不仅仅是儿童或年轻成人。

在有癌症遗传学家出席的专科MDT讨论后，偶尔可能适合在这些标准之外进行基因检测

重叠指征

R211 适用于应继续进行完整息肉病 panel 检测的息肉病患者

通路中的位置

申请专科

- 临床遗传学
- 手术
- 皮肤病学
- 肿瘤学*

* 包括儿科

专科服务组

- 核心

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R414.1	APC Associated Polyposis	Singleton	small variant detection, CNVs	Single gene	APC (1212)	Single gene sequencing ≥ 10 amplicons

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R414.1	APC相关息肉病	单人	小变异检测，拷贝数变异	单基因	APC（1212）	单基因测序 ≥ 10 扩增子

R212 Peutz Jeghers Syndrome

Testing Criteria

Living affected individual (proband) where the individual +/- family history meets one of the criteria.

1. ≥2 PJS-type hamartomatous polyps, OR
2. ≥1 PJS-type hamartomatous polyp and characteristic mucocutaneous pigmentation, OR
3. Characteristic mucocutaneous pigmentation age <10, OR
4. Sex cord tumours with annular tubules (SCAT) at any age
5. Adenoma malignum of the cervix at any age
6. ≥1 PJS-type hamartomatous polyp, AND ≥1 first / second degree relative with:
   a. ≥1 PJS-like feature, OR
   b. ≥2 PJS-related cancers (the two cancers can be in the same or different relatives), OR
7. Characteristic mucocutaneous pigmentation, AND ≥1 first / second degree relative with:
   a≥1 PJS-like feature, OR
   b. ≥2 PJS-related cancers (the two cancers can be in the same or different relatives)

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

PJS-like features: characteristic mucocutaneous pigmentation, PJS-type hamartomatous polyps

PJS-related cancers: epithelial colorectal, gastric, pancreatic, breast, and ovarian cancers, sex cord tumors with annular tubules (SCTAT), adenoma malignum of the cervix, and Sertoli cell tumors (LCST) of the testes

NOTE: The majority of polyps should be histologically confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Dermatology
- Gastroenterology
- Surgery

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R212.1	STK11 Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	STK11 (1377)	Single gene sequencing >=10 amplicons

R212PeutzJeghers综合征

检测标准

存活的患病个体(先证者)，其本人+/-家族史符合其中一项标准。

1. ≥2个PJS型错构瘤性息肉，或
2. ≥1个PJS型错构瘤性息肉和特征性皮肤黏膜色素沉着，或
3. 特征性皮肤黏膜色素沉着年龄<10岁,或
4. 任何年龄的环状小管性索肿瘤(SCAT)
5. 任何年龄的宫颈恶性腺瘤
6. ≥1个PJS型错构瘤性息肉，且≥1个一级/二级亲属患有：
   a. ≥1项PJS样特征，或
   b. ≥2种PJS相关癌症(这两种癌症可发生于同一或不同亲属)，或
7. 特征性皮肤黏膜色素沉着，且≥1名一级/二级亲属具有：a≥1项PJS样特征，或

   b. ≥2种PJS相关癌症(这两种癌症可发生于同一或不同亲属)

已故受累个体(先证者)，且满足以下所有条件；

(i)个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，

和

(iii) 无存活患病个体可供基因检测，且(iv)经专科癌症遗传学MDT讨论后

PJS样特征：特征性皮肤黏膜色素沉着、PJS型错构瘤性息肉

PJS相关癌症：上皮性结直肠癌、胃癌、胰腺癌、乳腺癌和卵巢癌，环状小管性索肿瘤(SCTAT)，宫颈恶性腺瘤，以及睾丸支持细胞瘤(LCST)

注：大多数息肉应经组织学确认

在特殊 MDT 讨论并有肿瘤遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

通路中的位置

初诊时/随访时

申请专科

- 临床遗传学
- 皮肤病学
- 胃肠病学
- 手术

专科服务组

- 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R212.1	STK11单基因测序	单人	小变异，拷贝数变异	单基因	STK11 (1377)	单基因测序 >=10扩增子

R213 PTEN Hamartoma Tumour Syndrome

Testing Criteria

Living affected individual (proband) where the individual +/- family history meets ONE of the criteria.

1. Macrocephaly AND Mucocutaneous lesions comprising one of the following:
   a. ≥ 6 facial papules, of which ≥ 3 are trichilemmoma,
   b. Cutaneous facial papules AND oral mucosal papillomatosis,
   c. Oral mucosal papillomatosis AND acral keratosis,
   d. ≥6 palmoplantar keratosis.
2. Macrocephaly AND ≥1 major criteria
3. Macrocephaly AND ≥ 3 minor criteria
4. Cerebellar dysplastic gangliocytoma (Adult Lhermitte-Duclos disease (LDD))
5. Cleveland Clinic PTEN risk calculator score corresponding to probability of pathogenic/likely pathogenic variant of 10%

PTEN-HTS-related mucocutaneous lesions comprise:

- Cutaneous facial papules, including trichilemmomas
- Oral mucosal papillomatosis
- Acral (dorsal) keratoses
- Palmoplantar keratoses

Major criteria:

- Breast cancer
- Epithelial thyroid cancer (non-medullary)
- Macrocephaly (occipital frontal circumference ≥97th percentile)
- Endometrial carcinoma

Minor criteria:

- Other thyroid lesions (e.g., adenoma, multinodular goitre)
- Intellectual disability (IQ ≤75)
- Hamartomatous intestinal polyps
- Fibrocystic disease of the breast
- Lipomas
- Fibromas
- Genitourinary tumours (especially renal cell carcinoma)
- Genitourinary malformation
- Uterine fibroids
- Oesophageal glycogenic acanthosis

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

R213PTEN错构瘤肿瘤综合征检测标准

存活的患病个体(先证者)，其本人+/-家族史符合其中一项标准。1. 大头畸形且皮肤黏膜病变包括以下之一：

a. ≥ 6个面部丘疹，其中≥ 3个为毛鞘瘤，
b. 面部皮肤丘疹 AND 口腔黏膜乳头状瘤病，
c. 口腔黏膜乳头状瘤病 AND 肢端角化病，
d. ≥6 掌跖角化病。

2. 大头畸形 AND ≥1 项主要标准
3. 巨头畸形且≥ 3项次要标准
4. 小脑发育不良性神经节细胞瘤(成人 Lhermitte-Duclos 病(LDD))
5. Cleveland Clinic PTEN风险计算器评分对应致病性/可能致病性变异概率为10%

PTEN-HTS相关的皮肤黏膜病变包括：

• 面部皮肤丘疹，包括毛根鞘瘤
• 口腔黏膜乳头状瘤病
• 肢端(背侧)角化病
• 掌跖角化病

主要标准：

• 乳腺癌
• 上皮性甲状腺癌(非髓样)
• 大头畸形(枕额围 ≥97百分位)
• 子宫内膜癌

次要标准：

• 其他甲状腺病变(如腺瘤、多结节性甲状腺肿)
• 智力障碍(IQ ≤75)
• 错构瘤性肠息肉
• 乳腺纤维囊性病
• 脂肪瘤
• 纤维瘤
• 泌尿生殖系统肿瘤(尤其是肾细胞癌)
• 泌尿生殖系统畸形
• 子宫肌瘤
• 食管糖原棘皮症

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

在特殊 MDT 讨论并有肿瘤遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Dermatology
- Neurology

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R213.1	PTEN Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	PTEN (1382)	Single gene sequencing >=10 amplicons

通路中的位置

初诊时/随访时

申请专科

• 临床遗传学

• 皮肤病学

• 神经科

专科服务组

• 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R213.1	PTEN单基因测序	单人	小变异，拷贝数变异	单基因	PTEN (1382)	单基因测序 >=10扩增子

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R214 Nevoid Basal Cell Carcinoma Syndrome or Gorlin syndrome

Testing Criteria

1. Living individual affected (proband) where the individual history meets:
   a. ≥ 1 major OR
   b. ≥ 2 minor criteria
2. Major criteria:

- Lamellar (sheet-like) calcification of the falx or clear evidence of calcification in an individual younger than age 20 years
- Jaw keratocyst: odontogenic keratocyst histologically
- Palmar/plantar pits (two or more)
- SHH medulloblastoma, confirmed on tumour testing
- Multiple basal cell carcinomas (BCCs) (>5 under 50)

3. Minor criteria:

- Childhood medulloblastoma where SHH pathway in tumour has not been investigated (also called primitive neuroectodermal tumor [PNET])
- Lympho-mesenteric or pleural cysts
- Macrocephaly (OFC >97th centile)
- Cleft lip/palate
- Vertebral/rib anomalies observed on chest x-ray and/or spinal x-ray; bifid/splayed/extra ribs; bifid vertebrae
- Preaxial or postaxial polydactyly
- Ovarian/cardiac fibromas
- Ocular anomalies (cataract, developmental defects, and pigmentary changes of the retinal epithelium)

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Dermatology

R214痣样基底细胞癌综合征或Gorlin综合征检测标准

1. 受累活体个体(先证者)，其个人史符合：
   a. ≥ 1 个主要 OR
   b. ≥ 2 项次要标准
2. 主要标准：

• 大脑镰层状(片状)钙化或较年轻个体中明确的钙化证据
超过20岁

• 颌骨角化囊肿：组织学上为牙源性角化囊肿

• 掌/跖凹(两个或更多)

• SHH 髓母细胞瘤，经肿瘤检测确认

• 多发性基底细胞癌(BCCs)(50岁以下超过5个)

3. 次要标准：

• 儿童期髓母细胞瘤，肿瘤中SHH通路未进行检测(也称为原始神经外胚层肿瘤[PNET])

• 淋巴肠系膜囊肿或胸膜囊肿

• 大头畸形(OFC >97百分位)

• 唇裂/腭裂

• 胸部X线和/或脊柱X线观察到椎骨/肋骨异常；分叉/张开/额外肋骨；分叉椎骨

• 轴前或轴后多指(趾)

• 卵巢/心脏纤维瘤

• 眼部异常(白内障、发育缺陷和视网膜上皮色素改变)

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

在特殊 MDT 讨论并有肿瘤遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

通路中的位置

初诊时/随访时

申请专科

• 临床遗传学

• 皮肤病学

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R214.1	PTCH1; SUFU	Singleton	Small variants, CNVs	Small panel	PTCH1; SUFU (1373)	Small panel

专科服务组

• 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R214.1	PTCH1；SUFU	单人	小变异，拷贝数变异	小检测板	PTCH1；SUFU (1373)	小检测板

R215 Hereditary diffuse gastric cancer

Testing Criteria

1. Living affected individual (proband) where the individual +/- family history **meets one of the criteria**. The proband has:
   a. Diffuse gastric cancer (<50 years).
   b. gastric in situ signet ring cells or pagetoid spread of signet ring cells under 50 years
   c. diffuse gastric cancer at any age with a personal history or FDR with cleft lip or cleft palate.
   d. double primary diffuse gastric cancer and lobular breast cancer (both <70 years).
   e. diffuse gastric cancer at any age and ≥ 1 FDR/SDR with diffuse gastric cancer at any age.
   f. diffuse gastric cancer at any age and ≥1 FDR/SDR with lobular breast cancer <70 years.
   g. Lobular breast cancer and ≥1 FDR/SDR with diffuse gastric cancer < 70 years.
   h. Two or more cases of lobular breast cancer < 50 years e.g. multiple ipsilateral tumours in proband or LBC < 50 years in two or more First/Second Degree relatives.
   i. Bilateral lobular breast cancer < 70 years
   j. diffuse gastric cancer in any individual of Maori ethnicity

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

NOTE: At least one cancer should be histologically confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Gastroenterology
- Surgery*

*Surgery to cover upper gastro-intestinal surgeons

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R215.1	Hereditary diffuse gastric cancer	Singleton	Small variants, CNVs	Small panel	CDH1; CTNNA1 (1221)	Small panel

R215遗传性弥漫性胃癌

检测标准

1. 存活的患病个体(先证者)，其本人+/-家族史**符合其中一项标准**。先证者具有：
   a. 弥漫性胃癌(<50岁)。
   b. 胃原位印戒细胞或50岁以下印戒细胞派杰样播散
   c. 任何年龄的弥漫性胃癌，伴有唇裂或腭裂的个人史或FDR。
   d. 双原发弥漫性胃癌和小叶乳腺癌(均<70岁)。
   e. 任何年龄的弥漫性胃癌且≥1名FDR/SDR在任何年龄患有弥漫性胃癌。
   f. 任何年龄的弥漫性胃癌且≥1名FDR/SDR在<70岁患有小叶乳腺癌。
   g. 小叶乳腺癌且≥1名一级/二级亲属患弥漫性胃癌< 70岁。
   h. 两例或以上<50岁小叶乳腺癌,例如先证者多发同侧肿瘤或两名或以上一级/二级亲属<50岁患LBC。
   i. 双侧小叶乳腺癌< 70岁
   j. 任何毛利族个体的弥漫性胃癌

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

注：至少有一种癌症应经组织学确诊

在特殊 MDT 讨论并有肿瘤遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

通路中的位置

初诊时/随访时

申请专科

- 临床遗传学
- 胃肠病学
- 手术*

* 以涵盖上消化道外科医生

专科服务组

- 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R215.1	遗传性弥漫性胃癌	单人	小变异，拷贝数变异	小检测板	CDH1；CTNNA1 (1221)	小检测板

R216 Li Fraumeni Syndrome

Testing Criteria

Living affected individual (proband) where the individual +/- family history meets **ONE** of the criteria.

The proband has:

1. Rhabdomyosarcoma (≤ 5 years),
2. Rhabdomyosarcoma of embryonal anaplastic subtype (any age)
3. Adrenocortical cancer (any age),
4. Choroid plexus cancer (any age),
5. Breast cancer (≤ 30 years),
6. HER2 positive breast cancer (≤ 35 years),
7. Hypodiploid acute lymphoblastic leukaemia (<18 years)
8. SHH medulloblastoma (<18 years)
9. Jaw osteosarcoma (<18 years)
10. ≥2 LFS-related cancers (both occurring ≤ 46 years; two breast cancers not eligible),
11. ≥1 LFS-related cancer with ≥1 first / second degree relative with ≥1 LFS-related cancer (one case ≤ 46 years, the other case ≤ 56 years; two breast cancers not eligible),
12. Cancer with ≥2 first / second degree relatives with cancer; across the family there is:
    i. 1 individual with sarcoma ≤ 45 years, AND
    ii. 1 individual with any cancer ≤ 45 years, AND
    iii. 1 individual with either a sarcoma OR any cancer occurring ≤ 45 years

13. Proband with personal history of 2 or more POT1-associated cancers (cutaneous melanoma, chronic lymphocytic leukaemia, angiosarcoma, glioma but excluding two cases of cutaneous melanoma) OR Proband with POT1 associated cancer and ≥1 FDR/SDR affected with a POT1 associated cancer (excluding two cases of cutaneous melanoma)

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

LFS-related cancers comprise: soft tissue sarcomas, osteosarcomas, adrenocortical carcinoma, central nervous system tumours and breast cancers including malignant phylloides tumours.

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- The relevant cancer clinical indication (M coded) should be used for somatic testing (TP53)

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Oncology*

*including paediatrics

Specialist Service Group

- Inherited cancer

R216李弗劳梅尼综合征

检测标准

存活的患病个体(先证者)，其本人+/-家族史符合**一项**标准。先证者具有：

1. 横纹肌肉瘤(≤ 5岁),
2. 胚胎性间变性亚型横纹肌肉瘤(任何年龄)
3. 肾上腺皮质癌(任何年龄),
4. 脉络丛癌(任何年龄),
5. 乳腺癌(≤ 30岁),
6. HER2阳性乳腺癌(≤35岁),
7. 低二倍体急性淋巴细胞白血病(<18岁)
8. SHH型髓母细胞瘤(<18岁)
9. 颌骨骨肉瘤(<18岁)
10. ≥2种LFS相关癌症(两者均发生于≤46岁；两例乳腺癌不符合),
11. ≥1种LFS相关癌症且≥1名一级/二级亲属患有≥1种LFS相关癌症(一例≤46岁，另一例≤56岁；两例乳腺癌不符合),
12. 癌症且≥2名一级/二级亲属患有癌症；整个家族中存在：
    i. 1 例肉瘤患者 ≤ 45 岁，且
    ii. 1 例任何癌症 ≤ 45 岁的个体，且
    iii. 1 例患有肉瘤或在 ≤ 45 岁发生任何癌症的个体
13. 先证者有2种或以上POT1相关癌症的个人史(皮肤黑色素瘤、慢性淋巴细胞白血病、血管肉瘤、胶质瘤，但排除两例皮肤黑色素瘤)或

先证者患有POT1相关癌症，且≥1名一级/二级亲属患POT1相关癌症(排除两例皮肤黑色素瘤)已故患病个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

LFS相关癌症包括：软组织肉瘤、骨肉瘤、肾上腺皮质癌、中枢神经系统肿瘤和乳腺癌(包括恶性叶状肿瘤)。

注：先证者的癌症以及家族中报告的大多数癌症应已得到确认

在专科MDT讨论并有癌症遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的人员。重叠指征

• 相关的癌症临床指征(M编码)应用于体细胞检测(TP53)

通路中的位置

初诊时/随访时

申请专科

• 临床遗传学

• 肿瘤学*

* 包括儿科

专科服务组

• 遗传性癌症

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R216.1	Li Fraumeni Syndrome (1222) - small panel	Singleton	Small variants, CNVs	Small panel	TP53, POT1(1222)	Small panel

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R216.1	李-佛美尼综合征 (1222) - 小panel	单人	小变异，拷贝数变异	小检测板	TP53、POT1(1222)	小检测板

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R219 Retinoblastoma

Testing Criteria

Testing of phenotypically affected individual where the proband has Retinoblastoma (unilateral, bilateral or multifocal) +/- family history. RB1 somatic test can be undertaken instead in tumour material where indicated.

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

Testing in most patients will be arranged as part of management at one of the Highly Specialised Retinoblastoma Services

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present.

Overlapping indications

- M166 Retinoblastoma (paediatric) or the relevant cancer clinical indication (M coded) should be used for somatic testing

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Inherited cancer

Associated Tests

Please note all the tests below will be undertaken for R219 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R219.1	RB1 Single gene sequencing	Singleton	Small variants	Single gene(s)	RB1 (1384)	Single gene sequencing >=10 amplicons
R219.2	RB1 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	RB1 (1384)	MLPA or equivalent

R219视网膜母细胞瘤

检测标准

对表型受累个体进行检测，其中先证者患有视网膜母细胞瘤(单侧、双侧或多灶性)+/-家族史。在有指征的情况下，可改为在肿瘤材料中进行RB1体细胞检测。

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

大多数患者的检测将作为高度专业化视网膜母细胞瘤服务管理的一部分进行安排

检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的人员

在专科MDT讨论并有癌症遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。

重叠指征

• M166视网膜母细胞瘤(儿童)或相关的癌症临床指征(M编码)应用于体细胞检测

通路中的位置

初诊时/随访时

申请专科

• 临床遗传学

专科服务组

• 遗传性癌症

相关检测

请注意，对于R219临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R219.1	RB1单基因测序	单人	小变异	单基因	RB1(1384)	单基因测序 >=10扩增子
R219.2	RB1 MLPA或等效	单人	外显子水平拷贝数变异	单基因	RB1(1384)	MLPA或等效

R456 Embryonal tumour of possible germline origin

Testing Criteria

Living individual with any of the following:

1) Wilms tumour, multiple nephrogenic rests or nephroblastomatosis with **ONE** or more of the following:

1. Diagnosis <2 years, OR
2. Bilateral disease, OR
3. Multifocal disease, OR
4. Family history of Wilms tumour, OR
5. Unexplained proteinuria or renal failure, OR
6. Hypospadias, undescended testes or ambiguous genitalia, OR
7. Gonadoblastoma

2) Neuroblastoma

AND

1. Bilateral neuroblastoma, or multiple neuroblastoma, OR
2. One or more FDR/SDR/TDR with neuroblastoma, OR
3. Hirschsprung's or FDR/SDR/TDR with Hirschsprung's in FDR/SDR/TDR, OR
4. Congenital hypoventilation or FDR/SDR/TDR with congenital hypoventilation

3) Medulloblastoma <25 with subgroup sonic hedgehog (MB-SHH) where other germline panel or paired WGS has not been undertaken

4) Atypical teratoid/rhabdoid tumour OR Small cell carcinoma of the ovary, hypercalcaemic type (SCCOHT) (any age)

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Oncology
- Clinical Genetics

Specialist Service Group

- Inherited cancer

Associated Tests – next page

Please note all the tests below will be undertaken for R456 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

R456胚胎性肿瘤可能胚系起源

检测标准

活体个体具有以下任一情况：

1) **Wilms瘤**、多发性肾源性残余或肾母细胞瘤病，伴以下**一项**或多项：

1. 诊断<2岁,或
2. 双侧病变，OR
3. 多灶性疾病，OR
4. 肾母细胞瘤家族史，或
5. 不明原因的蛋白尿或肾功能衰竭，或
6. 尿道下裂、未降睾丸或外生殖器性别不清，或
7. 性腺母细胞瘤

2) 神经母细胞瘤和

1. 双侧神经母细胞瘤，或多发性神经母细胞瘤，或
2. 一名或多名一级/二级/三级亲属患有神经母细胞瘤，或
3. 先天性巨结肠，或一级/二级/三级亲属患有先天性巨结肠，或
4. 先天性低通气或FDR/SDR/TDR伴先天性低通气

3)髓母细胞瘤<25岁,伴 sonic hedgehog 亚组(MB-SHH),且未进行其他胚系 panel 或配对 WGS

4)非典型畸胎样/横纹肌样瘤或卵巢小细胞癌，高钙血症型(SCCOHT)(任何年龄)

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

初诊时/随访时

申请专科

• 肿瘤学

• 临床遗传学

专科服务组

• 遗传性癌症

相关检测-下一页

请注意，对于R456临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R456.1	Embryonal tumour of possible germline origin	Singleton	SNVs, CNVs	Panel of genes or loci	ALK, BUB1B, CBL, CDKN1C, CTR9, DICER1, DIS3L2, ELP1, EZH2, GPC3, GPR161, HRAS, ISCA-37401-loss, KRAS, PHOX2B, PTCH1, PTPN11, REST, SMARCA4, SMARCB1, SOS1, SUFU, TP53, TRIM28, TRIM37, TRIP13, WT1 Embryonal tumour of possible germline origin (1636)	Medium panel
R456.2	Embryonal tumour of possible germline origin	Singleton	Methylation CNVs	Single interval	11p15 imprinted growth regulatory region	Methylation testing

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R456.1	胚胎性肿瘤 可能为胚系 来源	单人	SNVs、CNVs	基因检测板或 基因座	ALK、BUB1B、CBL、CDKN1C、CTR9、DICER1、DIS3L2、ELP1、EZH2、GPC3、GPR161、HRAS、ISCA-37401-缺失，KRAS，PHOX2B，PTCH1，PTPN11，REST，SMARCA4，SMARCB1，SOS1，SUFU，TP53，TRIM28，TRIM37，TRIP13，WT1 可能源于生殖系的胚胎性肿瘤 (1636)	中检测板
R456.2	胚胎性肿瘤 可能为胚系 来源	单人	甲基化 拷贝数变异	单一区间	11p15印记生长 调控区域	甲基化检测

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R457 Sarcoma of possible germline origin

Testing Criteria

Living individual with any of the following AND where other germline panel or paired WGS has not been undertaken:

Sarcoma

- Translocation negative sarcoma <25
  OR
- Sarcoma and one or more FDR/SDR with sarcoma any age
  OR
- Multiple primary sarcomas
  OR
- Malignant peripheral nerve sheath tumour <25

Chordoma

- Chordoma <25
  OR
- Multiple chordomas
  OR
- Chordoma and one or more FDR/SDR with chordoma any age
  OR
- Multiple benign notochordal tumour / ecchordosis physaliphora

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Oncology
- Clinical Genetics

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R457	Sarcoma of possible germline origin	Singleton	SNVs, CNVs	Panel of genes or loci	BUB1B, CBL, DICER1, HRAS, KRAS, NBS1, NF1, PTPN11, RB1, RECQL2, RECQL4, TBXT duplications, RECQL2, TP53 Sarcoma of possible germline origin (1637)	Small panel

R457肉瘤可能胚系起源

检测标准

存活个体，具有以下任一情况，且未进行其他胚系 panel 或配对 WGS:

肉瘤

• 易位阴性肉瘤<25
  或
• 肉瘤及一名或多名任何年龄患肉瘤的一级/二级亲属
  或
• 多原发肉瘤
  或
• 恶性外周神经鞘瘤<25

脊索瘤

• 脊索瘤 <25
  或
• 多发性脊索瘤
  或
• 脊索瘤及一名或多名任何年龄患脊索瘤的一级/二级亲属
  或
• 多发性良性脊索瘤/颅内脊索残余

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

通路中的位置

初诊时/随访时

申请专科

• 肿瘤学
• 临床遗传学

专科服务组

• 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R457	肉瘤可能为胚系来源	单人	SNVs、CNVs	基因检测板或基因座	BUB1B、CBL、DICER1、HRAS KRAS、NBS1、NF1、PTPN11 RB1、RECQL2、RECQL4、TBXT 重复，RECQL2,TP53 可能具有生殖系起源的肉瘤 (1637)	小检测板

R224 Inherited renal cancer

Testing Criteria

Testing of individual (proband) affected with renal cancer where the individual +/- family history meets one of the following criteria. The proband has

1. Renal cancer (≤ 46 years), OR
2. FH deficient/HLRCC-associated Renal Cell Carcinoma OR SDH-deficient RCC OR
3. Bilateral/multifocal renal cancer (any age), OR
4. A renal cancer AND first degree relative with renal cancer, both cases diagnosed under 60 years of age
5. Renal cancer AND second degree relative with renal cancer, both cases diagnosed under 50 years of age
6. Renal tumour and features of inherited cancer syndrome such as:
    - Cerebellar/spinal haemangioblastoma
    - Retinal angioma
    - Phaeochromocytoma/paraganglioma
    - Spontaneous pneumothorax and/or characteristic radiological features of Birt-Hogg-Dubé syndrome on chest imaging
    - Fibrofolliculomas
    - Trichodiscomas
    - Cutaneous Leiomyomata
    - Uterine leiomyomas (under 40 years of age with pathology suggesting FH variant)
    - Mesothelioma
    - Uveal melanoma

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

Referral to Clinical Genetics is required for karyotype in families with ≥3 FDR/SDR with renal cancer following MDT discussion

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M18 Renal cell carcinoma or the associated paediatric cancer clinical indication (M173, M180, M165, M212) should be used for somatic testing

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Urology

Nephrology

R224遗传性肾癌

检测标准

对患肾癌的个体(先证者)进行检测，其中个体+/-家族史满足以下标准之一。先证者具有

1. 肾癌(≤ 46岁)，或
2. FH 缺陷型/HLRCC 相关肾细胞癌或 SDH 缺陷型 RCC 或
3. 双侧/多灶性肾癌(任何年龄)，或
4. 肾癌且一级亲属患肾癌，两例均在60岁以下确诊
5. 肾癌且二级亲属患肾癌，两例均在50岁以下确诊
6. 肾肿瘤及遗传性癌症综合征特征，例如：
    - o 小脑/脊髓血管母细胞瘤 o 视网膜血管瘤
    - o 嗜铬细胞瘤/副神经节瘤
    - o 自发性气胸和/或Birt-Hogg-Dubé特征性影像学表现 胸部影像学上的综合征
    - o 纤维毛囊瘤
    - o 毛盘瘤
    - o 皮肤平滑肌瘤
    - o 子宫平滑肌瘤(40岁以下，病理提示FH变异)o 间皮瘤
    - o 葡萄膜黑色素瘤

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

对于≥3名一级/二级亲属患肾癌的家族，经MDT讨论后需转诊至临床遗传学进行核型分析

注：先证者的癌症以及家族中报告的大多数癌症应已得到确认

在专科MDT讨论并有癌症遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的人员。重叠指征

- M18 肾细胞癌或相关的儿童癌症临床指征(M173、M180、M165、M212)应用于体细胞检测

通路中的位置

初诊时/随访时

申请专科

- 临床遗传学
- 泌尿科

肾脏病学

Specialist Service Group

Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R224.1	Inherited renal cancer Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Inherited renal cancer (521)	Small panel

专科服务组

遗传性肿瘤

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R224.1	遗传性肾癌症小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	遗传性肾癌 (521)	小检测板

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R225 Von Hippel Lindau syndrome

Testing Criteria

Testing of individual (proband) affected with VHL-related tumours where the individual/family history meets one of the following criteria:

a. Retinal angioma, spinal or endolymphatic sac tumour (<40 years), OR
b. Cerebellar OR spinal haemangioblastoma (<60 years), OR
c. ≥2 VHL-related tumours (any age), OR
d. ≥1 VHL-related tumour and a first degree relative with ≥1 VHL-related tumour (where one of the tumours is retinal angioma / hemangioblastoma)

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND
(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND
(iii) no living affected individual is available for genetic testing, AND
(iv) after discussion at specialist cancer genetics MDT

VHL-related tumours comprise: Retinal angioma, Spinal or cerebellar hemangioblastoma, adrenal or extra-adrenal pheochromocytoma, Renal cell carcinoma, multiple renal and/or pancreatic cysts, endolymphatic sac tumors, papillary cystadenomas of the epididymis or broad ligament, neuroendocrine tumour of the pancreas

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Nephrology
- Neurology
- Ophthalmology
- Urology
- Neurosurgery

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R225.1	VHL Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	VHL (1403)	Single gene sequencing >=10 amplicons

R225VonHippelLindau综合征

检测标准

对患有VHL相关肿瘤且个体/家族史符合以下条件的个体(先证者)进行检测

符合以下标准之一：

a.视网膜血管瘤、脊髓或内淋巴囊肿瘤(<40岁),或 b.小脑或脊髓血管母细胞瘤(<60岁),
或

c. ≥2个VHL相关肿瘤(任何年龄)，或
d. ≥1个VHL相关肿瘤且有一名一级亲属患有≥1个VHL相关肿瘤(其中之一的肿瘤为视网膜血管瘤/血管母细胞瘤)

已故受累个体(先证者)，且满足以下所有条件；

(i)个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，

和

(iii) 无存活患病个体可供基因检测，且(iv)经专科癌症遗传学MDT讨论后

VHL相关肿瘤包括：视网膜血管瘤、脊髓或小脑血管母细胞瘤、肾上腺或肾上腺外嗜铬细胞瘤、肾细胞癌、多发性肾和/或胰腺囊肿、内淋巴囊肿瘤、附睾或阔韧带乳头状囊腺瘤、胰腺神经内分泌肿瘤

注：先证者的癌症以及家族中报告的大多数癌症应已得到确认

在特殊 MDT 讨论并有肿瘤遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

通路中的位置

初诊时/随访时

申请专科

- 临床遗传学
- 内分泌学
- 肾脏科
- 神经科
- 眼科
- 泌尿科
- 神经外科

专科服务组

- 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R225.1	VHL单基因测序	单人	小变异，拷贝数变异	单基因	VHL(1403)	单基因测序 >=10扩增子

R254 Familial melanoma

Testing Criteria

Testing of phenotypically affected individual (proband) where the individual +/- family history meets **ONE** of the following criteria. The proband has:

a. ≥1 melanoma < 18 years
b. ≥2 melanomas and/or melanomas in situ age <30 years,
c. One melanoma <30 years AND ≥ 1 First Degree Relative / Second Degree Relative <30
d. ≥3 melanoma and/or melanomas in situ at any age,
e. Total of ≥3 melanoma across the proband (who must have at least 1) and first degree/second degree relatives
f. ≥ 2 Melanoma and/or melanoma in situ AND ≥1 first degree relative with pancreatic cancer aged <60
g. Melanoma and/or melanoma in situ AND atypical moles AND ≥1 first degree relative with pancreatic cancer aged <60,

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M7 Melanoma (adult) and M187 Uveal melanoma should be used for somatic testing

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R254.1	Familial melanoma Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Familial melanoma (522)	Small panel

R254家族性黑色素瘤

检测标准

对表型受累个体(先证者)进行检测，其中个体+/-家族史符合以下标准中的**一项**。先证者具有：

a. ≥1例黑色素瘤< 18岁
b. ≥2 个黑色素瘤和/或原位黑色素瘤，年龄<30 岁,
c. 一个<30岁的黑色素瘤且≥1名<30岁的一级亲属/二级亲属
d. 任何年龄出现≥3个黑色素瘤和/或原位黑色素瘤，
e. 先证者(必须至少有1个)和一级/二级亲属中总共≥3个黑色素瘤
f. ≥2个黑色素瘤和/或原位黑色素瘤且≥1名一级亲属患有<60岁的胰腺癌
g. 黑色素瘤和/或原位黑色素瘤且非典型痣且≥1名一级亲属患有<60岁的胰腺癌,

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

在专科MDT讨论并有癌症遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的人员。重叠指征

• M7 黑色素瘤(成人)和 M187 葡萄膜黑色素瘤应用于体细胞检测

通路中的位置

初诊时/随访时

申请专科

• 临床遗传学
• 皮肤病学

专科服务组

• 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R254.1	家族性黑色素瘤小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	家族性黑色素瘤 (522)	小检测板

R422 BAP1 associated tumour predisposition syndrome

Testing Criteria

Individual has ONE of the following:

1. Individual with a personal history of two or more core BAP1 associated tumours (mesothelioma, uveal melanoma, cutaneous melanoma, renal cell cancer or BAP1 inactivated melanocytic tumour- BIMT) (excluding two cases of melanoma)
2. Individual with a personal history of two or more inactivated melanocytic tumours (BIMT) (Also known as BAPoma, atypical Spitz naevus, Melanocytic BAP1-associated intradermal tumor (MBAIT) or nevoid melanoma-like melanocytic proliferation (NEMMP)
3. Individual with a personal history of a BAP1 associated tumour and a first degree relative with a BAP1 core associated tumour (mesothelioma, uveal melanoma, cutaneous melanoma, renal cell cancer or BAP1 inactivated melanocytic tumour- BIMt) (excluding two cases of melanoma or renal cancer)
4. Individual with mesothelioma (less than 60 years) in the absence of asbestos exposure
5. Individual with uveal melanoma (<40 years)

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

BAP1 associated tumours= uveal melanoma, cutaneous melanoma, basal cell cancer, BAP1-inactivated melanocytic tumors (BIMT), malignant mesothelioma (lung or peritoneal), renal cell carcinoma, meningioma, cholangiocarcinoma or hepatocellular carcinoma.

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

R254 Familial melanoma

R214 Nevoid Basal Cell Carcinoma Syndrome or Gorlin syndrome

R224 Inherited renal cancer

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Dermatology
- Oncology

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R422.1	BAP1 associated tumour predisposition syndrome	Singleton	Small variants, CNVs	Single gene	BAP1 (1216)	Single gene sequencing >=10 amplicons

R422BAP1相关肿瘤易感性综合征

检测标准

个体符合以下任一情况：

1. 具有两种或以上核心BAP1相关肿瘤(间皮瘤、葡萄膜黑色素瘤、皮肤黑色素瘤、肾细胞癌或BAP1失活黑色素细胞肿瘤-BIMT)个人史的个体(排除两例黑色素瘤)
2. 具有两种或以上失活黑色素细胞肿瘤(BIMT)个人史的个体(又称BAPoma、非典型Spitz痣、黑色素细胞BAP1相关真皮内肿瘤(MBAIT)或痣样黑色素瘤样黑色素细胞增生(NEMMP))
3. 具有BAP1相关肿瘤个人史且有一名一级亲属患有BAP1核心相关肿瘤(间皮瘤、葡萄膜黑色素瘤、皮肤黑色素瘤、肾细胞癌或BAP1失活黑色素细胞肿瘤-BIMT)的个体(排除两例黑色素瘤或肾癌)
4. 无石棉暴露的间皮瘤个体(小于60岁)
5. 葡萄膜黑色素瘤患者(<40岁)

已故受累个体(先证者)，且满足以下所有条件；

(i)个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，

和

(iii) 无存活患病个体可供基因检测，且(iv)经专科癌症遗传学MDT讨论后

BAP1相关肿瘤=葡萄膜黑色素瘤、皮肤黑色素瘤、基底细胞癌、BAP1失活黑色素细胞肿瘤(BIMT)、恶性间皮瘤(肺或腹膜)、肾细胞癌、脑膜瘤、胆管癌或肝细胞癌。

在特殊 MDT 讨论并有肿瘤遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的个体。

重叠指征 R254 家族性黑色素瘤

R214 痣样基底细胞癌综合征或Gorlin综合征

R224 遗传性肾癌

通路中的位置

初诊时/随访时

申请专科

- 临床遗传学
- 皮肤病学
- 肿瘤学

专科服务组

- 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R422.1	BAP1相关肿瘤易感性综合征	单人	小变异，拷贝数变异	单基因	BAP1 (1216)	单基因测序 >=10扩增子

R363 Inherited predisposition to GIST

Testing Criteria

Testing of affected individual (proband) where the individual +/- family history meets the following criteria:
The proband has GIST (gastrointestinal stromal tumour):

1. Diagnosed age before age 50, OR
2. With ≥1 relative (first / second / third degree relative) with GIST, phaeochromocytoma / paraganglioma

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M8 Gastrointestinal stromal tumour should be used for somatic testing
- R223 Inherited phaeochromocytoma and paraganglioma excluding NF1

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Gastroenterology

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R363.1	Inherited predisposition to GIST Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Inherited predisposition to GIST (523)	Small panel

R363遗传性易感性至GIST

检测标准

对患病个体(先证者)进行检测，其中该个体+/-家族史符合以下标准：
先证者患有 GIST(胃肠道间质瘤):

1. 诊断年龄在50岁之前，或
2. 具有≥1名亲属(一级/二级/三级亲属)患有GIST、嗜铬细胞瘤/副神经节瘤

注：先证者的癌症以及家族中报告的大多数癌症应已得到确认

已故受累个体(先证者)，且满足以下所有条件；

(i)个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，

和

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

在有癌症遗传学家出席的专科MDT讨论后，偶尔可能适合在这些标准之外进行基因检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

• M8 胃肠间质瘤应用于体细胞检测

• R223 遗传性嗜铬细胞瘤和副神经节瘤(不包括NF1)

通路中的位置

初诊时/随访时

申请专科

• 临床遗传学

• 内分泌学

• 胃肠病学

专科服务组

• 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R363.1	遗传性易感性 GIST 小panel	单人	小变异，拷贝数变异	基因检测板或基因座	遗传性GIST易感性 (523)	小检测板

R364 DICER1-related cancer predisposition

Testing Criteria

1. Testing of affected individual (proband) where the individual has one of the following diagnoses:

Pleuropulmonary blastoma or Lung cyst(s) in childhood, especially if multi-septated, multiple or bilateral; Thoracic, uterine, cervical or ovarian embryonal rhabdomyosarcoma; Cystic nephroma; Genitourinary sarcoma including undifferentiated sarcoma in childhood; Ovarian Sertoli Leydig tumour; Gynandroblastoma; Genitourinary/gynaecologic neuroendocrine tumors; Childhood-onset multinodular goitre or differentiated thyroid cancer (papillary or follicular); Ciliary body medulloepithelioma; Nasal chondromesenchymal hamartoma; Pineoblastoma; Pituitary blastoma, OR

2. Testing of affected individual where there is a combination of two of the following diagnoses, either both in one affected individual or in two affected first degree relatives;

Lung cyst(s) in adults; Wilms tumor; Multinodular goiter or differentiated thyroid cancer; Embryonal rhabdomyosarcoma other than thoracic or gynaecologic; Poorly differentiated neuroendocrine tumour; Undifferentiated sarcoma; Macrocephaly

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M245 Ovarian sex cord stromal tumours

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Paediatric oncology
- Paediatric endocrinology

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R364.1	DICER1 related cancer predisposition Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	DICER1 (1320)	Single gene sequencing >=10 amplicons

R364DICER1相关癌症易感性

检测标准

1. 对患病个体(先证者)进行检测，其中该个体具有以下诊断之一：

胸膜肺母细胞瘤或儿童期肺囊肿，尤其是多分隔、多发或双侧；

胸部、子宫、宫颈或卵巢胚胎性横纹肌肉瘤；囊性肾瘤；泌尿生殖系统肉瘤包括儿童期未分化肉瘤；卵巢Sertoli Leydig肿瘤；

两性母细胞瘤；泌尿生殖/妇科神经内分泌肿瘤；儿童期发病的多结节性甲状腺肿或分化型甲状腺癌(乳头状或滤泡状)；

睫状体髓上皮瘤；鼻腔软骨间叶错构瘤；松果体母细胞瘤；垂体母细胞瘤，或

2. 对患病个体进行检测，其中存在以下诊断中两种的组合，或两者
在一个受累个体或两个受累一级亲属中；

成人肺囊肿；Wilms瘤；多结节性甲状腺肿或分化型甲状腺癌；非胸部或妇科的胚胎性横纹肌肉瘤；低分化神经内分泌肿瘤；未分化肉瘤；大头畸形

已故受累个体(先证者)，且满足以下所有条件；

(i)个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，

和

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

注：先证者的癌症以及家族中报告的大多数癌症应已得到确认

在有癌症遗传学家出席的专科MDT讨论后，偶尔可能适合在这些标准之外进行基因检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

- M245 卵巢性索间质肿瘤

通路中的位置

初诊时/随访时

申请专科

- 临床遗传学
- 儿童肿瘤学
- 儿科内分泌科

专科服务组

- 遗传性癌症

相关检测

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R364.1	DICER1相关癌症易感性 单基因测序	单人	小检测板变异，拷贝数变异	单基因	DICER1 (1320)	单基因测序 ≥10个扩增子

R365 Fumarate hydratase-related tumour syndromes

Testing Criteria

Testing of affected individual (proband) with hereditary leiomyomatosis and renal cell cancer (HLRCC) or other FH deficiency disorder where the individual +/- family history meets one of the following criteria. The proband has:

a. Type 2 papillary, HLRCC associated RCC (WHO pathology definition) OR tubulo-papillary renal tumour at any age, OR

b. Two of: cutaneous leiomyomata, renal tumour (any histology), uterine leiomyomata with classic histological features and/or FH deficiency (any age) OR

c. Cutaneous leiomyomata AND one first / second / third degree relative with renal tumour, OR

d. Cutaneous leiomyomata AND two first / second / third degree relatives with cutaneous leiomyomata OR uterine leiomyomata with classic histological features < 40 years, OR

e. Uterine leiomyomata with classic histological features (age <40) OR

f. Multiple cutaneous leiomyomata

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

NOTE: Cutaneous leiomyomata should be histologically confirmed; uterine leiomyomata and renal tumours should be medically documented

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M18 Renal cell carcinoma or the associated pediatric cancer clinical indication (M173, M180, M165, M212) should be used for somatic testing
- M246 Uterine smooth muscle tumours

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Dermatology
- Urology
- Nephrology

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R365.1	FH Single gene sequencing	Singleton	Small variants	Single gene(s)	FH (1335)	Single gene sequencing >=10 amplicons

R365延胡索酸水合酶相关肿瘤综合征

检测标准

对患有遗传性平滑肌瘤病和肾细胞癌(HLRCC)的患病个体(先证者)进行检测，或

其他FH缺陷疾病，其中该个体+/-家族史符合以下标准之一。先证者具有：

a. 2型乳头状、HLRCC相关RCC(WHO病理学定义)或任何年龄的管状乳头状肾肿瘤，或

b. 以下两项：皮肤平滑肌瘤、肾肿瘤(任何组织学)、具有典型组织学特征的子宫平滑肌瘤和/或FH缺陷(任何年龄)，或

c. 皮肤平滑肌瘤且有一名一级/二级/三级亲属患有肾肿瘤，或

d. 皮肤平滑肌瘤且有两名一级/二级/三级亲属患有皮肤平滑肌瘤或具有典型组织学特征的子宫平滑肌瘤<40岁,或

e. 具有典型组织学特征的子宫平滑肌瘤(年龄<40岁)或

f. 多发性皮肤平滑肌瘤

已故受累个体(先证者)，且满足以下所有条件；

(i)个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，

和

(iii) 无存活患病个体可供基因检测，且(iv)经专科癌症遗传学MDT讨论后

注：皮肤平滑肌瘤应经组织学确认；子宫平滑肌瘤和肾肿瘤应有医学记录

在专科MDT讨论并有癌症遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的人员。重叠指征

- M18 肾细胞癌或相关儿童癌症临床指征(M173、M180、M165、M212)应用于体细胞检测
- M246 子宫平滑肌肿瘤

通路中的位置

初诊时/随访时

申请专科

- 临床遗传学
- 皮肤病学
- 泌尿科
- 肾脏科

专科服务组

- 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R365.1	FH单基因测序	单人	小变异	单基因	FH (1335)	单基因测序 >=10扩增子

R367 Inherited pancreatic cancer

Testing Criteria

Testing of affected individual (proband) where the individual +/- family history meets one of the following criteria. The proband has:

1. Pancreatic cancer age <60, OR
2. Pancreatic cancer age <70, AND
   a. Breast cancer age <60, melanoma age <60, OR ovarian cancer, OR
   b. One first / second degree relative with pancreatic cancer age <60, OR
   c. Two or more first / second degree relatives with any of breast cancer age <60, melanoma age <60, OR ovarian cancer OR two or more with pancreatic cancer (any age)

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

NOTE: The proband's cancer and majority of reported cancers in the family should have been confirmed. Pancreatic cancer is adenocarcinoma and not neuroendocrine tumour.

If there is a family history of BRCA related cancers (breast, ovarian, prostate and pancreatic), please consider if R208 Inherited Breast Cancer panel testing is required.

If there is a family history of melanoma, please consider if R254 Familial Melanoma panel testing is required.

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M219 Pancreatic cancer should be used for somatic testing

Where in Pathway

At presentation/at follow-up

Requesting Specialties

- Clinical Genetics
- Gastroenterology
- Oncology

Specialist Service Group

- Inherited cancer

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R367.1	Inherited pancreatic cancer Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Inherited pancreatic cancer (524)	Small panel

R367遗传性胰腺癌

检测标准

对患病个体(先证者)进行检测，其中该个体+/-家族史符合以下之一标准。先证者具有：

1. 胰腺癌年龄<60,或
2. 胰腺癌年龄<70,且
   a. 乳腺癌发病年龄<60岁、黑色素瘤发病年龄<60岁,或卵巢癌,或
   b. 一名一级/二级亲属患有胰腺癌且年龄<60岁,或
   c. 两名或以上一级/二级亲属患有以下任何疾病：乳腺癌年龄<60岁、黑色素瘤年龄<60岁,或卵巢癌,或两名或以上患有胰腺癌(任何年龄)

已故受累个体(先证者)，且满足以下所有条件；

(i)个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，

和

(iii) 无存活患病个体可供基因检测，且(iv)经专科癌症遗传学MDT讨论后

注：先证者的癌症和家族中报告的大多数癌症应已确认。胰腺癌为腺癌而非神经内分泌肿瘤。

如有BRCA相关癌症(乳腺、卵巢、前列腺和胰腺)家族史，请考虑是否需要R208遗传性乳腺癌panel检测。

如有黑色素瘤家族史，请考虑是否需要R254家族性黑色素瘤panel检测。

在专科MDT讨论并有癌症遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的人员。重叠指征

• M219 胰腺癌应使用体细胞检测

通路中的位置

初诊时/随访时

申请专科

• 临床遗传学
• 胃肠病学
• 肿瘤学

专科服务组

• 遗传性癌症

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R367.1	遗传性胰腺癌小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	遗传性胰腺癌 (524)	小检测板

R404 Testing of unaffected individuals for inherited cancer predisposition syndromes

Testing Criteria

Germline testing of unaffected individuals for specific inherited cancer predisposition syndromes where the following criteria are met:

1. There are no living affected relatives available for testing, AND
2. Any applicable somatic testing on deceased relatives tumour samples has been performed first, AND
3. The individual to be tested is deemed to have ≥10% chance of having a monogenic variant (deceased first degree relative with ≥20% chance), AND
4. This is agreed by specialist cancer genetics MDT

For testing for hereditary breast and ovarian cancer and inherited MMR deficiency (Lynch syndrome), unaffected individuals must meet criteria as specified under relevant indications R208/R215

NOTE: All cancers must be confirmed

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Core and Inherited cancer; depending on the cancer of suspicion

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R404.1	Inherited cancer predisposition gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	As dictated by clinical indication	Single gene sequencing >=10 amplicons
R404.3	Relevant inherited cancer panel Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Relevant inherited cancer panel	Small panel

R404检测的未患病个体针对遗传性癌症易感性综合征

检测标准

对未患病个体进行特定遗传性癌症易感综合征的胚系检测，需满足以下标准：

1. 没有在世患病亲属可供检测，且
2. 已首先对已故亲属的肿瘤样本进行任何适用的体细胞检测，且
3. 被检测个体被认为具有≥10%的携带单基因变异的机会(已故一级亲属具有≥20%的机会)，且
4. 这是由专科癌症遗传学MDT所认可的

对于遗传性乳腺癌和卵巢癌及遗传性MMR缺陷(Lynch综合征)的检测，未患病个体必须符合相关指征R208/R215下规定的标准

注意：所有癌症均须经确认

在有癌症遗传学家出席的专科MDT讨论后，偶尔可能适合在这些标准之外进行基因检测

通路中的位置

申请专科

• 临床遗传学

专科服务组

• 核心与遗传性癌症；取决于疑似癌症类型

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R404.1	遗传性癌症易感基因测序	单人	小变异，拷贝数变异	单基因	根据临床指征决定	单基因测序 >=10扩增子
R404.3	相关遗传性癌症panel 小型检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	相关遗传性癌症panel	小检测板

R430 Inherited prostate cancer

Testing Criteria

- Proband diagnosed with prostate cancer at <50 years
- Ashkenazi Jewish ancestry and prostate cancer at any age
- ≥1 grandparent from Whalsay (Shetland) and prostate cancer at any age
- Proband diagnosed with metastatic prostate cancer <60 years
- Proband diagnosed with prostate cancer with a CanRisk score of >10% and where they do not meet criteria for R208, R207 or R210 - see overlapping Clinical Indications

Deceased affected individual (proband) where all the following are met;

(i) the individual +/- family history meets one of the above criteria, AND

(ii) a previously stored constitutional blood/DNA or tissue sample (tumour or normal) is available, AND

(iii) no living affected individual is available for genetic testing, AND

(iv) after discussion at specialist cancer genetics MDT

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present.

Overlapping indications

- R208 Inherited breast cancer and ovarian cancer - Proband affected with prostate cancer who has a personal/family history of other BRCA related cancers see R208 (BRCA related cancers = breast, ovarian, pancreatic, prostate).
- R207 Inherited ovarian cancer (without breast cancer)
- R210 Inherited MMR deficiency (Lynch syndrome) - For prostate cancer with personal/family history of other Lynch related cancers see R210 (See list of Lynch related cancers in R210).
- R444 NICE approved PARP inhibitor treatment
- M218 prostate cancer should be used for somatic testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Oncology
- Urology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R430.1	Inherited prostate cancer	Singleton	Small variants, CNVs	Small panel of genes	Inherited prostate cancer (1223)	Small panel

R430遗传性前列腺癌症

检测标准

- 先证者在<50岁时被诊断为前列腺癌
- 德系犹太人血统及任何年龄的前列腺癌
- ≥1 祖父母来自 Whalsay(设得兰)，且在任何年龄患前列腺癌
- 先证者确诊为转移性前列腺癌，年龄<60岁
- 先证者被诊断为前列腺癌，CanRisk评分>10%，且不符合R208、R207或R210的标准--参见重叠的临床指征

已故受累个体(先证者)，且满足以下所有条件；

(i)该个体+/-家族史符合上述标准之一，且(ii)有先前储存的体质性血液/DNA或组织样本(肿瘤或正常)可用，且

(iii) 无存活受累个体可供进行基因检测，且

(iv)经专科癌症遗传学 MDT 讨论后

在专科MDT讨论并有癌症遗传学家在场的情况下，偶尔可能适合在这些标准之外进行基因检测。

重叠指征

- R208 遗传性乳腺癌和卵巢癌 - 先证者患有前列腺癌，且有其他BRCA相关癌症的个人史/家族史，参见R208(BRCA相关癌症=乳腺、卵巢、胰腺、前列腺)。
- R207 遗传性卵巢癌(无乳腺癌)
- R210 遗传性MMR缺陷(Lynch综合征)- 对于前列腺癌且有其他Lynch相关癌症个人史/家族史者，参见R210(Lynch相关癌症列表见R210)。
- R444 NICE 批准的 PARP 抑制剂治疗
- M218 前列腺癌应使用于体细胞检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 肿瘤学
- 泌尿科

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R430.1 遗传性前列腺癌症		单人	小变异，拷贝数变异	小检测板基因	遗传性前列腺癌(1223)	小检测板

R444 NICE approved PARP inhibitor treatment

Testing Criteria

Testing Criteria only applies to patients not meeting R208/R430 criteria AND with current cancer diagnosis for treatment decisions.

R444.1 Breast Cancer

1. For people with triple negative breast cancer who have received neo-adjuvant chemotherapy: residual invasive cancer in the breast, the resected lymph nodes (non-pathological complete response) or both at the time of surgery
2. For people with triple-negative breast cancer having adjuvant chemotherapy:
    - node-positive OR
    - node-negative cancer with a primary tumour ≥ 2 cm
3. For people with hormone receptor-positive, HER2-negative breast cancer who have received neoadjuvant chemotherapy:
    - residual invasive cancer in the breast, the resected lymph nodes (non-pathologic complete response) or both at the time of surgery, AND
    - either diagnostic or surgical specimen which is confirmed as pathological high grade ,
4. For people with hormone receptor-positive, HER2-negative breast cancer having adjuvant chemotherapy:
    - . a pre-chemotherapy pathological demonstration of at least one positive lymph node
5. For people who have HER2-negative locally advanced or metastatic breast cancer:
    - Patients should have been previously treated with an anthracycline and/or a taxane in the neo/adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments.
    - Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine-based therapy, or be considered unsuitable for endocrine-based therapy.

R444.2 Prostate Cancer

Metastatic, castration-resistant prostate cancer where somatic tumour testing (M218.1) has failed.

Overlapping indications

- R208 Inherited breast cancer and ovarian cancer
- R430 Inherited prostate cancer
- M3 breast cancer should be used for somatic testing
- M218 prostate cancer should be used for somatic testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At earliest stage, either at primary surgery or after neo-adjuvant chemotherapy

Requesting Specialties

- Clinical Genetics
- Surgery
- Oncology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R444.1	NICE approved PARP inhibitor treatment – breast cancer	Singleton	Small variants, CNVs	Small panel of genes	BRCA1; BRCA2;	Small panel
R444.2	NICE approved PARP inhibitor treatment – prostate cancer	Singleton	Small variants, CNVs	Small panel of genes	BRCA1, BRCA2	Small panel

R444NICE批准的PARP抑制剂治疗

检测标准

检测标准仅适用于不符合R208/R430标准且当前有癌症诊断以用于治疗决策的患者。

R444.1 乳腺癌

1. 对于接受过新辅助化疗的三阴性乳腺癌患者：手术时乳腺内残留浸润性癌、切除的淋巴结内残留浸润性癌(非病理学完全缓解)或两者兼有
2. 对于接受辅助化疗的三阴性乳腺癌患者：
    - 淋巴结阳性或
    - 原发肿瘤 ≥ 2 cm 的淋巴结阴性癌症
3. 对于接受过新辅助化疗的激素受体阳性、HER2阴性乳腺癌患者：
    - 手术时乳腺内残留浸润性癌、切除的淋巴结内残留浸润性癌(非病理学完全缓解)或两者兼有，且
    - 诊断性或手术标本被确认为病理学高级别，
4. 对于接受辅助化疗的激素受体阳性、HER2阴性乳腺癌患者：
    - 化疗前病理学证实至少一个阳性淋巴结
5. 对于HER2阴性局部晚期或转移性乳腺癌患者：
    - 患者应先前在新辅助/辅助、局部晚期或转移性治疗背景下接受过蒽环类和/或紫杉烷类治疗，除非患者不适合这些治疗。
    - 激素受体(HR)阳性乳腺癌患者应先前接受过基于内分泌的治疗，或被认为不适合基于内分泌的治疗。

R444.2 前列腺癌

转移性去势抵抗性前列腺癌，且体细胞肿瘤检测(M218.1)已失败。

重叠指征

- R208 遗传性乳腺癌和卵巢癌
- R430 遗传性前列腺癌
- M3 乳腺癌应进行体细胞检测
- M218 前列腺癌应使用于体细胞检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在最早阶段，即在初次手术时或新辅助化疗后

申请专科

- 临床遗传学
- 手术
- 肿瘤学

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R444.1 NICE批准PARP抑制剂治疗	治疗 – 乳腺癌	单人	小变异，拷贝数变异	小检测板基因	BRCA1; BRCA2； 小检测板	
R444.2 NICE批准PARP抑制剂治疗	治疗 – 前列腺癌	单人	小变异，拷贝数变异	小检测板基因	BRCA1、BRCA2	小检测板

Part XII. Lipids

R134 Familial hypercholesterolaemia

Testing Criteria

Dutch (or Welsh) lipid clinic score >5, OR

Simon Broome criteria indicate possible FH (following assessment in a specialist Lipid Clinic or Familial Hypercholesterolaemia service)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Chemical Pathology
- Clinical Genetics
- Metabolic Medicine
- Paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R134.1	Familial hypercholesterolaemia Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Familial hypercholesterolaemia – targeted panel (772)	Small panel

第XII部分脂质

R134家族性高胆固醇血症

检测标准

荷兰(或威尔士)脂质门诊评分 >5，或

Simon Broome标准提示可能的FH(经专科脂质门诊或家族性高胆固醇血症服务评估后)

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 心脏病学
- 化学病理学
- 临床遗传学
- 代谢医学
- 儿科

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R134.1	家族性高胆固醇血症小panel	单人	小变异，拷贝数变异	基因检测板或基因座	家族性高胆固醇血症 – 靶向检测组合 (772)	小检测板

R324 Familial Chylomicronaemia Syndrome (FCS)

Testing Criteria

1. Fasting triglycerides >20mmol/L, AND
2. Exclusion of secondary causes of hypertriglyceridaemia e.g. excess alcohol, uncontrolled diabetes

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Chemical Pathology
- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R324.1	Familial Chylomicronaemia Syndrome (FCS) Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Lipoprotein lipase deficiency (527)	Small panel

R324家族性乳糜微粒血症综合征(FCS)

检测标准

1. 空腹甘油三酯 >20mmol/L，且

2. 排除高甘油三酯血症的继发性原因，例如过量饮酒、未控制的糖尿病。检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理者。

通路中的位置

就诊时

申请专科

- 心脏病学
- 化学病理学
- 临床遗传学
- 代谢医学

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R324.1	家族性乳糜微粒血症综合征(FCS)小pan	单人	小变异，拷贝数变异	基因检测板或基因座	脂蛋白脂肪酶缺乏症 (527)	小检测板

Part XIII. Metabolic

R380 Niemann Pick disease type C

Testing Criteria

Clinical and laboratory features characteristic of Niemann-Pick disease type C

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Please note all the tests below will be undertaken for R380 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R380.1	NPC1; NPC2	Singleton	Small variants	Small panel	NPC1; NPC2 (1347)	Small panel
R380.2	NPC1; NPC2 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	NPC1; NPC2 (1347)	MLPA or equivalent

第XIII部分代谢

R380NiemannPick病C型

检测标准

尼曼-匹克病C型的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学
• 代谢医学

专科服务组

• 代谢性

相关检测

请注意，对于R380临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R380.1	NPC1;NPC2	单人	小变异	小检测板	NPC1；NPC2 (1347)	小检测板
R380.2	NPC1；NPC2 MLPA或等效方法	单人	外显子水平拷贝数变异	单基因	NPC1；NPC2 (1347)	MLPA或等效

R98 Likely inborn error of metabolism

Testing Criteria

Clinical feature of a likely inborn error of metabolism where targeted testing is not possible

Testing Criteria for Semi-Rapid Testing

- Children or adults with a suspected likely inborn error of metabolism, where a rapid diagnosis will direct immediate treatment or medical care of the patient, and:

- Biochemical testing and/or enzyme analysis specifically points to one particular gene and condition, or to a subset of genes and conditions for which specific testing can be provided using a “slice” or small subset of genes of the R98.2 gene panel.

- This testing pathway is not intended as an exclusion test for patients with a broad differential diagnosis, and without a specific diagnosis from biochemical testing/enzyme analyses. These referrals will not be accepted and will be directed to the WGS route.

- The patient is either not eligible for the R14 pathway or Rapid R98 is considered to be the more appropriate test.

Overlapping indications

- Targeted tests for specific metabolic disorders should be used where clinical features or biochemical/enzyme testing results are rapidly available and strongly suggestive of the relevant disorder(s)

Where in Pathway

At presentation following clinically relevant, rapidly available investigations

Where in Pathway for Semi-Rapid Testing

At presentation following clinically relevant, rapidly available investigations. All cases must be agreed in advance with the testing laboratory.

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Requesting Specialties for Semi-Rapid Testing

- Clinical Genetics
- Metabolic Medicine
- Neurology
- Neonatology

Specialist Service Group

- Metabolic

Associated Tests

R98.3 is only for semi urgent testing

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R98.2	Inborn errors of metabolism WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Inborn errors of metabolism (467)	WGS
R98.3	Inborn errors of metabolism WES	Trio	Exon level CNVs, Small variants	Panel of genes or loci	Inborn errors of metabolism (467)	WES

R98可能的先天性代谢缺陷

检测标准

可能的先天性代谢缺陷的临床特征，且无法进行靶向检测

半快速检测标准

- 疑似可能的先天性代谢缺陷的儿童或成人，且快速诊断将直接指导患者的即时治疗或医疗照护，并且：

- 生化检测和/或酶分析明确指向某一特定基因和疾病，或指向可通过R98.2基因面板的“切片”或小部分基因子集提供特定检测的一组基因和疾病。

- 该检测路径不适用于具有广泛鉴别诊断且无生化检测/酶分析特定诊断的患者作为排除性检测。此类转诊将不被接受，并将被转介至WGS路径。

- 患者不符合R14路径的资格，或Rapid R98被认为是更合适的检测。

重叠指征

• 针对特定代谢性疾病的靶向检测应在临床特征或
生化/酶学检测结果可快速获得并强烈提示相关疾病

通路中的位置

就诊时，在完成临床相关且可快速获得的检查后

半快速检测路径中

在临床相关、可快速获得的检查后就诊时。所有病例必须事先与检测实验室达成一致。

申请专科进行半快速检测

• 临床遗传学
• 代谢医学
• 神经科
• 新生儿科

专科服务组

• 代谢性

相关检测

R98.3仅用于半紧急检测

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R98.2	先天性代谢缺陷全基因组测序（第一阶段）	三人组或单人	外显子水平 CNVs，小变异，短串联重复序列	基因检测板或基因座	先天性代谢缺陷 (467)	全基因组测序
R98.3	先天性代谢缺陷全外显子组测	三人组	外显子水平 CNVs，小变异	基因检测板或基因座	先天性代谢缺陷 (467)	全外显子组测序

R270 Smith-Lemli-Opitz syndrome

Testing Criteria

Clinical and biochemical features characteristic of Smith-Lemli-Opitz syndrome

Overlapping indications

- R98 Likely inborn error of metabolism, R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with atypical features in whom a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following biochemical testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Please note all the tests below will be undertaken for R270 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R270.1	DHCR7 Single gene sequencing	Singleton	Small variants	Single gene(s)	DHCR7 (1392)	Single gene sequencing >=10 amplicons
R270.2	DHCR7 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	DHCR7 (1392)	MLPA or equivalent

R270Smith-Lemli-Opitz综合征

检测标准

史密斯-莱姆利-奥皮茨综合征的临床和生化特征

重叠指征

• R98 可能为先天性代谢缺陷，R27 儿科疾病或 R89 超罕见及非典型
单基因疾病检测应用于具有非典型特征且正在考虑更广泛鉴别诊断的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

生化检测后就诊时

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

请注意，以下所有检测均将用于R270临床指征申请，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R270.1	DHCR7单基因测序	单人	小变异	单基因	DHCR7 (1392)	单基因测序 >=10扩增子
R270.2	DHCR7 MLPA或等效	单人	外显子水平拷贝数变异	单基因	DHCR7 (1392)	MLPA或等效

R231 Neuronal ceroid lipofuscinosis

Testing Criteria

Clinical and laboratory features characteristic of Neuronal ceroid lipofuscinosis including presence of vacuolate lymphocytes, presence of pathological inclusions on tissue biopsy or enzyme deficiency

Overlapping indications

- R271 Neuronal ceroid lipofuscinosis type 2 test should be considered where clinical features are specific to CLN2
- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following histological analysis and/or enzyme testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R231.2	Neuronal ceroid lipofuscinosis Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Neuronal ceroid lipofuscinosis (526)	Small panel

R231神经元蜡样脂褐素沉积症

检测标准

神经元蜡样脂褐素沉积症的临床和实验室特征，包括空泡化淋巴细胞的存在、组织活检中病理包涵体的存在或酶缺陷

重叠指征

- 当临床特征特异时，应考虑R271神经元蜡样脂褐素沉积症2型检测至 CLN2
- 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在组织学分析和/或酶学检测后就诊时

申请专科

- 临床遗传学
- 代谢医学
- 神经科

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R231.2	神经元蜡样脂褐质沉积症 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	神经元蜡样脂褐质沉积症 (526)	小检测板

R271 Neuronal ceroid lipofuscinosis type 2

Testing Criteria

Clinical and laboratory features characteristic of neuronal ceroid lipofuscinosis type 2

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following histological analysis and/or enzyme testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R271.1	TPP1 Single gene sequencing	Singleton	Small variants	Single gene(s)	TPP1 (1371)	Single gene sequencing >=10 amplicons

R271神经元蜡样脂褐素沉积症2型2

检测标准

神经元蜡样脂褐素沉积症2型的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在组织学分析和/或酶学检测后就诊时

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R271.1	TPP1单基因测序	单人	小变异	单基因	TPP1 (1371)	单基因测序 >=10扩增子

R334 Cystinosis

Testing Criteria

1. Paediatric presentation with nephropathic cystinosis, OR
2. Adult presentation with non-nephropathic cystinosis

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Gastroenterology
- Metabolic Medicine
- Nephrology
- Neurology
- Ophthalmology

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R334.1	CTNS Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	CTNS (1319)	Single gene sequencing >=10 amplicons

R334胱氨酸病

检测标准

1. 儿童期起病的肾病型胱氨酸贮积症，或
2. 成人起病的非肾病性胱氨酸病

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 胃肠病学
- 代谢医学
- 肾脏科
- 神经科
- 眼科

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R334.1	CTNS单基因测序	单人	小变异，拷贝数变异	单基因	CTNS (1319)	单基因测序 >=10扩增子

R335 Fabry disease

Testing Criteria

- In males: clinical and laboratory features characteristic of Fabry disease following alpha-galactosidase A enzyme testing
- In females: clinical features characteristic of Fabry disease

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following alpha-galactosidase A enzyme testing

Requesting Specialties

- Cardiology
- Clinical Genetics
- Dermatology
- Metabolic Medicine
- Nephrology
- Ophthalmology

Specialist Service Group

- Metabolic

Associated Tests

Please note all the tests below will be undertaken for R335 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R335.1	GLA Single gene sequencing	Singleton	Small variants	Single gene(s)	GLA (1323)	Single gene sequencing <10 amplicons
R335.2	GLA MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	GLA (1323)	MLPA or equivalent

R335Fabry病

检测标准

• 男性：α-半乳糖苷酶A后出现法布雷病特征的临床和实验室表现酶检测

• 女性：具有法布雷病特征的临床特征

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在α-半乳糖苷酶A酶检测之后

申请专科

• 心脏病学

• 临床遗传学

• 皮肤病学

• 代谢医学

• 肾脏科

• 眼科

专科服务组

• 代谢性

相关检测

请注意，以下所有检测均将针对R335临床指征请求进行，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R335.1	GLA单基因测序	单人	小变异	单基因	GLA（1323）	单基因测序 <10扩增子
R335.2	GLA MLPA或等效	单人	外显子水平拷贝数变异	单基因	GLA（1323）	MLPA或等效

R325 Lysosomal acid lipase deficiency

Testing Criteria

Biochemically established lysosomal acid lipase deficiency

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Chemical Pathology
- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R325.1	LIPA Single gene sequencing	Singleton	Small variants	Single gene(s)	LIPA (1354)	Single gene sequencing >=10 amplicons

R325溶酶体酸性脂肪酶缺乏症

检测标准

生化确诊的溶酶体酸性脂肪酶缺乏症

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 化学病理学

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R325.1	LIPA单基因测序	单人	小变异	单基因	LIPA（1354）	单基因测序 >=10扩增子

R323 Sitosterolaemia

Testing Criteria

Elevated plasma beta-sitosterol with development of xanthomata before the age of 30

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Chemical Pathology
- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R323.1	ABCG5; ABCG8	Singleton	Small variants	Small panel	ABCG5; ABCG8 (1391)	Small panel

R323谷固醇血症

检测标准

30岁前出现血浆β-谷甾醇升高并发展为黄色瘤

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 心脏病学
- 化学病理学
- 临床遗传学
- 代谢医学

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R323.1	ABCG5；ABCG8	单人	小变异	小检测板	ABCG5；ABCG8（1391）	小检测板

R286 Tay-Sachs disease

Testing Criteria

Clinical and laboratory features characteristic of Tay-Sachs disease

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R286.1	HEXA Single gene sequencing	Singleton	Small variants	Single gene(s)	HEXA (1396)	Single gene sequencing >=10 amplicons

R286Tay-Sachs病

检测标准

Tay-Sachs 病的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R286.1	HEXA单基因测序	单人	小变异	单基因	HEXA（1396）	单基因测序 >=10扩增子

R272 Gaucher disease

Testing Criteria

Clinical features and glucocerebrosidase activity indicative of Gaucher disease types 1, 2, or 3, including the perinatal lethal and cardiovascular subtypes.

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following enzyme testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology
- Cardiology

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R272.1	GBA Single gene sequencing	Singleton	Small variants	Single gene(s)	GBA (1336)	Single gene sequencing >=10 amplicons

R272戈谢病

检测标准

临床特征和葡萄糖脑苷脂酶活性指示戈谢病1型、2型或3型，包括围产期致死型和心血管亚型。

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经酶学检测后

申请专科

• 临床遗传学
• 代谢医学
• 神经科
• 心脏病学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R272.1	GBA单基因测序	单人	小变异	单基因	GBA(1336)	单基因测序 >=10扩增子

R273 Glycogen storage disease V

Testing Criteria

Clinical and laboratory features characteristic of Glycogen storage disease type V including:

1. Elevated baseline serum CK, AND
2. Characteristic lactate/lactate:ammonia profile after exercise

Overlapping indications

- Broader R274 Glycogen storage disease panel test should be used where a broader differential diagnosis of glycogen storage diseases is under consideration
- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Cardiology
- Clinical Genetics
- Hepatology
- Metabolic Medicine
- Neurology
- Paediatrics

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R273.1	PYGM Single gene sequencing	Singleton	Small variants	Single gene(s)	PYGM (1340)	Single gene sequencing >=10 amplicons

R273糖原贮积病V

检测标准

糖原贮积病V型特征的临床和实验室表现，包括：

1. 基线血清 CK 升高，AND
2. 运动后乳酸/乳酸：氨特征的概况

重叠指征

- 当鉴别诊断范围较广时，应使用更广泛的R274糖原贮积病panel检测
  糖原贮积病的诊断正在考虑中
- 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
  检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

- 心脏病学
- 临床遗传学
- 肝脏病学
- 代谢医学
- 神经科
- 儿科

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R273.1	PYGM单基因测序	单人	小变异	单基因	PYGM (1340)	单基因测序 >=10扩增子

R274 Glycogen storage disease

Testing Criteria

Clinical and laboratory features characteristic of Glycogen storage disease:

1. Persistent hypoglycaemia with other metabolic disorders excluded, AND one or more of the following
   a. Persistent hepatomegaly in childhood, OR
   b. Liver biopsy suggestive of glycogen storage disease, OR
   c. Neuromuscular presentation suggestive of glycogen storage disease, OR
   d. Affected first degree relative

OR

2. Glycogen accumulation in the relevant tissue, AND one or more of the following:
   a. Evidence of liver involvement: hepatomegaly OR hypoglycaemia with other metabolic disorders excluded, OR
   b. Evidence of muscle involvement: myalgia OR rhabdomyolysis OR muscle weakness, OR
   c. Evidence of cardiac involvement: cardiomegaly OR cardiomyopathy, OR
   d. Other general evidence - at least two of: myopathy, cardiomyopathy, respiratory weakness, vacuolar myopathy on muscle biopsy, pathological pattern on oligosaccharides

Overlapping indications

- R273 Glycogen storage disease V test should be considered where clinical features are specific to Glycogen storage disease V (McArdle disease)
- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Cardiology
- Clinical Genetics
- Hepatology
- Metabolic Medicine
- Neurology
- Paediatrics

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R274.1	Glycogen storage disease WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Glycogen storage disease (528)	WES or Medium Panel

R274糖原贮积病检测标准

糖原贮积病的临床和实验室特征：

1.持续性低血糖且排除其他代谢性疾病，AND以下一项或多项

a.儿童期持续性肝大，OR b.肝活检提示糖原贮积病，OR c.神经肌肉表现提示糖原贮积病，OR d.受累一级亲属

或

2. 相关组织中糖原蓄积，并且具备以下一项或多项：
   a. 肝脏受累证据：肝大OR低血糖且排除其他代谢性疾病，OR
   b. 肌肉受累证据：肌痛或横纹肌溶解或肌无力，或
   c. 心脏受累的证据：心脏增大或心肌病，或
   d. 其他一般证据--至少两项：肌病、心肌病、呼吸肌无力、肌活检空泡性肌病、寡糖病理模式

重叠指征

• 当临床特征特异于糖原贮积病V型(McArdle病)时，应考虑R273糖原贮积病V型检测

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 心脏病学
• 临床遗传学
• 肝脏病学
• 代谢医学
• 神经科
• 儿科

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R274.1	糖原贮积病 WES 或中通量面板	单人	小变异，拷贝数变异	基因检测板或基因座	糖原贮积病(528) WES或Medium	检测板

R276 Lysosomal storage disorder

Testing Criteria

1. Clinical phenotype or radiological signs suggesting a lysosomal storage disorder, AND
2. Abnormal urine MPS or oligosaccharides screen or white cell enzymes analysis that are indicative of lysosomal storage disorder but do not allow more targeted testing

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R276.1	Lysosomal storage disorder WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Lysosomal storage disorder (529)	WES or Medium Panel

R276溶酶体贮积病

检测标准

1. 临床表型或影像学征象提示溶酶体贮积病，AND
2. 异常尿液MPS或寡糖筛查或白细胞酶分析指示
   溶酶体贮积病，但不允许进行更具针对性的检测

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学
• 代谢医学
• 神经科

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R276.1	溶酶体贮积疾病 WES 或中通量面板	单人	小变异，拷贝数变异	基因检测板或基因座	溶酶体贮积症 (529)	WES或Medium检测板

R288 GM1 Gangliosidosis and Mucopolysaccharidosis Type IVB

Testing Criteria

Clinical and laboratory features characteristic of GM1 Gangliosidosis or Mucopolysaccharidosis Type IVB

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R288.1	GLB1 Single gene sequencing	Singleton	Small variants	Single gene(s)	GLB1 (1341)	Single gene sequencing >=10 amplicons

R288GM1神经节苷脂沉积症和黏多糖贮积症IVB型

检测标准

GM1神经节苷脂沉积症或黏多糖贮积症IVB型特征的临床和实验室表现

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R288.1	GLB1单基因测序	单人	小变异	单基因	GLB1（1341）	单基因测序 >=10扩增子

R277 Mucopolysaccharidosis type IH/S

Testing Criteria

Clinical and laboratory features characteristic of Mucopolysaccharidosis type IH/S (Hurler-Scheie syndrome)

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R277.1	IDUA Single gene sequencing	Singleton	Small variants	Single gene(s)	IDUA (1360)	Single gene sequencing >=10 amplicons

R277黏多糖贮积症IH/S型

检测标准

黏多糖贮积症IH/S型(Hurler-Scheie综合征)特征的临床和实验室表现

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R277.1	IDUA单基因测序	单人	小变异	单基因	IDUA(1360)	单基因测序 >=10扩增子

R280 Krabbe disease – GALC deficiency

Testing Criteria

Clinical and laboratory features characteristic of Krabbe disease due to GALC deficiency

Overlapping indications

- R281 Krabbe disease - Saposin A deficiency should be used in individuals with clinical and laboratory features characteristic of atypical Krabbe disease due to Saposin A deficiency
- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Please note all the tests below will be undertaken for R280 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R280.1	GALC Single gene sequencing	Singleton	Small variants	Single gene(s)	GALC (1351)	Single gene sequencing >=10 amplicons
R280.2	GALC MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	GALC (1351)	MLPA or equivalent

R280Krabbe病-GALC缺乏症

检测标准

GALC缺乏所致Krabbe病特征的临床和实验室表现

重叠指征

- R281 Krabbe病 - Saposin A缺乏症应适用于具有临床和实验室由于Saposin A缺乏所致的非典型Krabbe病特征性表现
- 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

- 临床遗传学
- 代谢医学

专科服务组

- 代谢性

相关检测

请注意，以下所有检测均将针对R280临床指征请求进行，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R280.1	GALC单基因测序	单人	小变异	单基因	GALC（1351）	单基因测序 >=10扩增子
R280.2	GALC MLPA或等效	单人	外显子水平拷贝数变异	单基因	GALC（1351）	MLPA或等效

R281 Krabbe disease - Saposin A deficiency

Testing Criteria

Clinical and laboratory features characteristic of atypical Krabbe disease due to Saposin A deficiency

Overlapping indications

- R280 Krabbe disease – GALC deficiency should be used in individuals with clinical and laboratory features characteristic of atypical Krabbe disease due to GALC deficiency
- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R281.1	PSAP Single gene sequencing	Singleton	Small variants	Single gene(s)	PSAP (1352)	Single gene sequencing >=10 amplicons

R281Krabbe病-SaposinA缺乏症

检测标准

Saposin A缺乏所致非典型Krabbe病特征的临床和实验室表现

重叠指征

- R280 Krabbe病 - GALC缺乏症应适用于具有临床和实验室
  由于GALC缺乏导致的非典型Krabbe病特征性表现
- 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
  检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

- 临床遗传学
- 代谢医学

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R281.1	PSAP单基因测序	单人	小变异	单基因	PSAP（1352）	单基因测序 >=10扩增子

R278 Mucopolysaccharidosis type II

Testing Criteria

Clinical and laboratory features characteristic of Mucopolysaccharidosis type II

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Cleft clinics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Please note all the tests below will be undertaken for R278 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R278.1	IDS Single gene sequencing	Singleton	Small variants	Single gene(s)	IDS (1361)	Single gene sequencing >=10 amplicons
R278.2	IDS Targeted variant testing	Singleton	Small variants	Single gene(s)	IDS (1361)	Targeted variant testing

R278黏多糖贮积症II型

检测标准

黏多糖贮积症II型的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 唇腭裂门诊

• 代谢医学

专科服务组

• 代谢性

相关检测

请注意，以下所有检测均将针对R278临床指征请求进行，除非临床表现和/或初始结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R278.1	IDS单基因测序	单人	小变异	单基因	IDS（1361）	单基因测序 >=10扩增子
R278.2	IDS靶向变异检测	单人	小变异	单基因	IDS（1361）	靶向变异检测

R287 Mucopolysaccharidosis type IVA

Testing Criteria

Clinical and laboratory features characteristic of Mucopolysaccharidosis type IVA

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R287.1	GALNS Single gene sequencing	Singleton	Small variants	Single gene(s)	GALNS (1364)	Single gene sequencing >=10 amplicons

R287黏多糖贮积症IVA型

检测标准

黏多糖贮积症IVA型的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学
• 代谢医学
• 神经科

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R287.1	GALNS单基因测序	单人	小变异	单基因	GALNS (1364)	单基因测序 >=10扩增子

R289 Mucolipidosis II and III Alpha/Beta

Testing Criteria

Clinical and laboratory features characteristic of Mucolipidosis II or Mucolipidosis III Alpha/Beta

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R289.1	GNPTAB Single gene sequencing	Singleton	Small variants	Single gene(s)	GNPTAB (1359)	Single gene sequencing >=10 amplicons

R289黏脂贮积症II和IIIα/β

检测标准

黏脂贮积症II型或黏脂贮积症III型α/β的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R289.1	GNPTAB单基因测序	单人	小变异	单基因	GNPTAB (1359)	单基因测序 >=10扩增子

R290 Mucopolysaccharidosis type VI

Testing Criteria

Clinical and laboratory features characteristic of Mucopolysaccharidosis type VI

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R290.1	ARSB Single gene sequencing	Singleton	Small variants	Single gene(s)	ARSB (1365)	Single gene sequencing >=10 amplicons

R290黏多糖贮积症VI型

检测标准

黏多糖贮积症VI型的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R290.1	ARSB单基因测序	单人	小变异	单基因	ARSB (1365)	单基因测序 >=10扩增子

R291 Mucopolysaccharidosis type IIIA

Testing Criteria

Clinical and laboratory features characteristic of Mucopolysaccharidosis type IIIA

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R291.1	SGSH Single gene sequencing	Singleton	Small variants	Single gene(s)	SGSH (1362)	Single gene sequencing >=10 amplicons

R291黏多糖贮积症IIIA型

检测标准

黏多糖贮积症IIIA型的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学
• 代谢医学
• 神经科

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R291.1	SGSH单基因测序	单人	小变异	单基因	SGSH (1362)	单基因测序 >=10扩增子

R292 Mucopolysaccharidosis type IIIB

Testing Criteria

Clinical and laboratory features characteristic of Mucopolysaccharidosis type IIIB

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R292.1	NAGLU Single gene sequencing	Singleton	Small variants	Single gene(s)	NAGLU (1363)	Single gene sequencing >=10 amplicons

R292黏多糖贮积症IIIB型

检测标准

黏多糖贮积症IIIB型的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学
• 代谢医学
• 神经科

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R292.1	NAGLU单基因测序	单人	小变异	单基因	NAGLU (1363)	单基因测序 >=10扩增子

R282 Niemann-Pick disease type A or B

Testing Criteria

Clinical and laboratory features characteristic of Niemann-Pick disease type A or B

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R282.1	SMPD1 Single gene sequencing	Singleton	Small variants	Single gene(s)	SMPD1 (1375)	Single gene sequencing >=10 amplicons

R282Niemann-Pick病A型或B

检测标准

Niemann-Pick病A型或B型的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R282.1	SMPD1单基因测序	单人	小变异	单基因	SMPD1 (1375)	单基因测序 >=10扩增子

R285 Sandhoff disease

Testing Criteria

Clinical and laboratory features characteristic of Sandhoff disease

Overlapping indications

- It is anticipated that many specific metabolic diagnoses will be made through use of broad genomic testing via the R98 Likely inborn error of metabolism early in the investigative pathway and in cases with atypical features where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following laboratory testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R285.1	HEXB Single gene sequencing	Singleton	Small variants	Single gene(s)	HEXB (1385)	Single gene sequencing >=10 amplicons

R285Sandhoff病

检测标准

Sandhoff病特有的临床和实验室特征

重叠指征

• 预计许多特定的代谢性疾病诊断将通过使用广泛的基因组
检测在检查路径早期通过R98可能的先天性代谢缺陷进行，以及在考虑更广泛鉴别诊断的非典型特征病例中

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，实验室检测后

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R285.1	HEXB单基因测序	单人	小变异	单基因	HEXB (1385)	单基因测序 >=10扩增子

R283 Phenylketonuria

Testing Criteria

1. Likely phenylketonuria identified following diagnostic metabolic testing **OR**
2. Testing patients diagnosed with PKU to indicate sapropterin responsiveness

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following neonatal screening or diagnostic metabolic testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R283.1	PAH Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	PAH (1378)	Single gene sequencing >=10 amplicons

R283苯丙酮尿症

检测标准

1.诊断性代谢检测后确定的可能苯丙酮尿症**或**
2. 对确诊为 PKU 的患者进行检测，以提示对沙丙蝶呤的反应性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在新生儿筛查或诊断性代谢检测之后

申请专科

• 临床遗传学

• 代谢医学

专科服务组

• 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R283.1	PAH单基因测序	单人	小变异，拷贝数变异	单基因	PAH (1378)	单基因测序 >=10扩增子

R450 Diagnostic testing for Isovaleric acidaemia

Testing Criteria

Likely isovaleric acidaemia identified following diagnostic metabolic testing where genetic testing is required as part of the diagnostic testing pathway.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Testing following newborn screening should follow the established sample and testing pathways set out in the newborn screening protocol and use code R279

Where in Pathway

Following diagnostic metabolic testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neonatology
- Obstetrics
- Paediatrics

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R450.1	Diagnostic testing for Isovaleric acidaemia	Singleton	Small variants	Single interval	IVD	Single gene sequencing >=10 amplicons

R450诊断性检测用于异戊酸血症

检测标准

诊断性代谢检测后确定的可能异戊酸血症，其中基因检测作为诊断检测路径的一部分被要求。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

新生儿筛查后的检测应遵循新生儿筛查方案中规定的既定样本和检测路径，并使用代码R279

通路中的位置

在诊断性代谢检测之后

申请专科

- 临床遗传学
- 代谢医学
- 新生儿科
- 产科
- 儿科

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R450.1	诊断检测用于异戊酸血症	单人	小变异	单一区间	IVD	单基因测序 >=10扩增子

R279 Isovaleric acidaemia newborn screening follow up

Testing Criteria

Likely isovaleric acidaemia identified following neonatal screening

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family. In the case of isovaleric acidaemia, this means that testing is almost exclusively used at those in whom biochemical results indicate a likely pseudodeficiency allele is present.

Testing following newborn screening should follow the established sample and testing pathways set out in the newborn screening protocol

Where in Pathway

Following neonatal screening

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neonatology
- Obstetrics
- Paediatrics

Specialist Service Group

- Screening

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R279.1	IVD common pseudodeficiency variant Targeted variant testing	Singleton	Small variants	Single interval	IVD common pseudodeficiency variant	Targeted variant testing

R279异戊酸血症新生儿筛查随访

检测标准

新生儿筛查后发现的疑似异戊酸血症

检测转诊将由基因组实验室进行分诊；检测应针对那些遗传或基因组诊断将指导先证者或家族管理的人群。对于异戊酸血症，这意味着检测几乎专门用于生化结果表明可能存在假性缺陷等位基因的人群。

新生儿筛查后的检测应遵循新生儿筛查方案中规定的既定样本和检测路径

通路中的位置

新生儿筛查后

申请专科

- 临床遗传学
- 代谢医学
- 新生儿科
- 产科
- 儿科

专科服务组

- 筛查

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R279.1	IVD常见假性缺陷变异靶向变异检测	单人	小变异	单一区间	IVD常见假性缺陷变异	靶向变异检测

R451 Diagnostic testing for MCADD - Medium-chain acyl-CoA dehydrogenase deficiency – full ACADM sequencing

Testing Criteria

Likely MCADD identified following diagnostic metabolic testing and where testing of common variants or full screen of the ACADM gene is required

Overlapping indications:

Testing following newborn screening should follow the established sample and testing pathways set out in the newborn screening protocol and use codes R105 and R403

Where in Pathway

Following diagnostic metabolic testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neonatology
- Paediatrics

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R451.1	Diagnostic testing for MCADD full ACADM sequencing	Singleton	Small variants	Other	ACADM (1355)	Single gene sequencing <10 amplicons

R451诊断性检测用于MCADD-中链酰基辅酶A脱氢酶缺乏症-完整ACADM测序

检测标准

诊断性代谢检测后确定的可能MCADD，且需要检测常见变异或ACADM基因全筛查

重叠指征：

新生儿筛查后的检测应遵循新生儿筛查方案中规定的既定样本和检测路径，并使用代码R105和R403

通路中的位置

在诊断性代谢检测之后

申请专科

- 临床遗传学
- 代谢医学
- 新生儿科
- 儿科

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R451.1	诊断检测用于MCADD完整ACADM测序	单人	小变异	其他	ACADM (1355)	单基因测序 <10扩增子

R105 MCADD - Medium-chain acyl-CoA dehydrogenase deficiency – common variant newborn screening follow up

Testing Criteria

Likely MCADD identified following neonatal screening requiring testing of the common ACADM c.985G>A variant

Testing following newborn screening should follow the established sample and testing pathways set out in the newborn screening protocol

Where in Pathway

Following neonatal screening

Requesting Specialties

- Clinical Genetics
- Neonatology
- Obstetrics
- Paediatrics

Specialist Service Group

- Screening

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R105.1	ACADM common pathogenic variants Targeted variant testing	Singleton	Small variants	Single interval	ACADM common pathogenic variants	Targeted variant testing

R105MCADD-中链酰基辅酶A脱氢酶缺乏症-常见变异新生儿筛查随访

检测标准

新生儿筛查后确定的可能MCADD，需要检测常见ACADM c.985G>A变异

新生儿筛查后的检测应遵循新生儿筛查方案中规定的既定样本和检测路径

通路中的位置

新生儿筛查后

申请专科

• 临床遗传学
• 新生儿科
• 产科
• 儿科

专科服务组

• 筛查

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R105.1	ACADM常见致病变异 靶向变异检测	单人	小变异	单一区间	ACADM常见致病变异	靶向变异检测

R403 MCADD - Medium-chain acyl-CoA dehydrogenase deficiency – full ACADM sequencing newborn screening follow up

Testing Criteria

Likely MCADD identified following neonatal screening requiring testing of the full ACADM gene

Overlapping indications:

- R105 MCADD - Medium-chain acyl-CoA dehydrogenase deficiency – common variant test should be used in the first instance except where the testing laboratory specifically guides otherwise

Testing following newborn screening should follow the established sample and testing pathways set out in the newborn screening protocol

Where in Pathway

N/A

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neonatology
- Paediatrics

Specialist Service Group

- Screening

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R403.1	MCADD Single gene sequencing	Singleton	Small variants	Other	ACADM (1355)	Single gene sequencing <10 amplicons

R403MCADD-中链酰基辅酶A脱氢酶缺乏症-完整ACADM测序新生儿筛查随访

检测标准

新生儿筛查后确定的可能MCADD，需要检测ACADM全基因

重叠指征：

• R105 MCADD - 中链酰基辅酶A脱氢酶缺乏症 - 常见变异检测应首先使用，除非检测实验室特别指导另有规定

新生儿筛查后的检测应遵循新生儿筛查方案中规定的既定样本和检测路径

通路中的位置

申请专科

• 临床遗传学
• 代谢医学
• 新生儿科
• 儿科

专科服务组

• 筛查

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R403.1	MCADD单次基因测序	单人	小变异	其他	ACADM (1355)	单基因测序 <10扩增子

R449 Diagnostic testing for Glutaric acidaemia I

Testing Criteria

Likely glutaric acidaemia type 1 identified following diagnostic metabolic testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Testing following newborn screening should follow the established sample and testing pathways set out in the newborn screening protocol and use code R275

Where in Pathway

Following diagnostic metabolic testing

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neonatology
- Obstetrics
- Paediatrics

Specialist Service Group

- Metabolic

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R449.1	GCDH Single gene sequencing	Singleton	Small variants	Single gene(s)	GCDH (1339)	Single gene sequencing >=10 amplicons

R449诊断性检测用于戊二酸血症I

检测标准

诊断性代谢检测后确定的可能戊二酸血症1型

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

新生儿筛查后的检测应遵循新生儿筛查方案中规定的既定样本和检测路径，并使用代码R275

通路中的位置

在诊断性代谢检测之后

申请专科

- 临床遗传学
- 代谢医学
- 新生儿科
- 产科
- 儿科

专科服务组

- 代谢性

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R449.1	GCDH单基因测序	单人	小变异	单基因	GCDH(1339)	单基因测序 >=10扩增子

R275 Glutaric acidaemia I newborn screening follow up

Testing Criteria

Likely glutaric acidaemia type 1 identified following neonatal screening

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Testing following diagnostic metabolic testing should use code R449 and follow the routing for specialist metabolic tests

Where in Pathway

Following neonatal screening

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neonatology
- Obstetrics
- Paediatrics

Specialist Service Group

- Screening

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R275.1	GCDH Single gene sequencing	Singleton	Small variants	Single gene(s)	GCDH (1339)	Single gene sequencing >=10 amplicons

R275戊二酸血症I新生儿筛查随访

检测标准

新生儿筛查后发现的可能戊二酸血症1型

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

诊断性代谢检测后的检测应使用代码R449并遵循专科代谢检测的路径

通路中的位置

新生儿筛查后

申请专科

• 临床遗传学
• 代谢医学
• 新生儿科
• 产科
• 儿科

专科服务组

• 筛查

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R275.1	GCDH单基因测序	单人	小变异	单基因	GCDH(1339)	单基因测序 >=10扩增子

Part XIV. Mitochondrial

R64 MELAS or MIDD

Testing Criteria

Adult onset sensorineural hearing loss and diabetes or family history suggestive of a diagnosis of maternally inherited diabetes and deafness OR

A clinical presentation compatible with MELAS ((Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R64.1	MTTL1 3243A>G Targeted variant testing	Singleton	Small variants	Single interval	MTTL1 3243A>G	Targeted variant testing

第XIV部分线粒体

R64MELAS或MIDD

检测标准

成人起病的感觉神经性听力损失和糖尿病，或提示母系遗传性糖尿病和耳聋诊断的家族史或

与MELAS（线粒体脑肌病、乳酸酸中毒和
中风样发作)
检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学
• 内分泌学
• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R64.1	MTTL1 3243A>G 靶向变异检测	单人	小变异	单一区间	MTTL1 3243A>G	靶向变异检测

R299 Possible mitochondrial disorder - mitochondrial DNA rearrangement testing

Testing Criteria

Possible mitochondrial disorder caused by mitochondrial DNA rearrangements including individuals with clinical features suggestive of CPEO, Kearns-Sayre syndrome or Pearson syndrome

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Affected tissue, such as muscle, preferred

Where in Pathway

At presentation following assessment by a Consultant in Metabolic Medicine, Neurology, Paediatric Neurology, Clinical Genetics or Haematology

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R299.1	Possible Mitochondrial disorder - Mitochondrial DNA rearrangement testing	Singleton	CNVs	Single interval	Mitochondrial genome	Other
R299.2	Possible mitochondrial disorder - mitochondrial DNA rearrangement testing	Singleton	CNVs and structural variants	Single interval	Heteroplasmy assessment - mitochondrial genome	Other
R299.3	Possible mitochondrial disorder - mitochondrial DNA rearrangement testing	Singleton	CNVs and structural variants	Single interval	Breakpoint mapping - mitochondrial genome	Other

R299可能的线粒体疾病-线粒体DNA重排检测

检测标准

由线粒体DNA重排导致的可能线粒体疾病，包括具有提示CPEO、Kearns-Sayre综合征或Pearson综合征临床特征的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理的个体。首选受累组织，如肌肉

通路中的位置

在代谢医学、神经病学、儿科神经病学、临床遗传学或血液学顾问评估后就诊时

申请专科

• 临床遗传学
• 代谢医学
• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R299.1	可能线粒体疾病 - 线粒体DNA重排检测	单人	拷贝数变异	单一区间	线粒体基因组	其他
R299.2	可能线粒体疾病 - 线粒体DNA重排检测	单人	CNVs和结构变异	单一区间	异质性评估 - 线粒体基因组	其他
R299.3	可能线粒体疾病 - 线粒体DNA重排检测	单人	CNVs和结构变异	单一区间	断点定位 - 线粒体基因组	其他

R300 Possible mitochondrial disorder - whole mitochondrial genome sequencing

Testing Criteria

Clinical features strongly suggestive of a mitochondrial disorder and/or biochemical evidence of a mitochondrial DNA disorder

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant in Metabolic Medicine, Neurology, Paediatric Neurology or Clinical Genetics, or following biochemical studies

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R300.1	Mitochondrial genome Whole mitochondrial genome sequencing	Singleton	Small variants	Single interval	Mitochondrial genome	Other

R300可能的线粒体疾病-全线粒体基因组测序

检测标准

强烈提示线粒体疾病的临床特征和/或线粒体DNA疾病的生化证据

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在代谢医学、神经病学、儿科神经病学或临床遗传学顾问评估后就诊时，或在生化研究后

申请专科

• 临床遗传学
• 代谢医学
• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R300.1	线粒体 基因组全 线粒体 基因组 测序	单人	小变异	单一区间	线粒体基因组	其他

R301 Possible mitochondrial disorder - mitochondrial DNA depletion testing

Testing Criteria

Clinical features suggestive of a mitochondrial DNA depletion syndrome

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Muscle or liver tissue required

Where in Pathway

Following findings on biopsy sample

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R301.1	Mitochondrial genome Mitochondrial DNA depletion testing	Singleton	Complex variants	Single interval	Mitochondrial genome	Other

R301可能的线粒体疾病-线粒体DNA耗竭检测

检测标准

提示线粒体DNA耗竭综合征的临床特征

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理的个体。需要肌肉或肝脏组织

通路中的位置

活检样本的以下发现

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R301.1	线粒体 基因组 线粒体DNA耗竭检	单人	复合体 变异	单一区间	线粒体基因组	其他

R315 POLG-related disorder

Testing Criteria

Clinical features suggestive of a POLG-related disorder (including status epilepticus and other severe intractable epilepsy with other suggestive features)

Overlapping indications

- R27 Paediatric disorders or other relevant broader tests should be used instead where clinical features are not strongly suggestive of POLG-related disorder and a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant in Metabolic Medicine, Neurology, Paediatric Neurology or Clinical Genetics, or following evidence of mtDNA depletion or multiple mtDNA deletions

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Please note all the tests below will be undertaken for R315 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R315.1	Common POLG variants Targeted variant testing	Singleton	Small variants	Single interval	Common POLG variants	Targeted variant testing
R315.2	POLG Single gene sequencing	Singleton	Small variants	Single gene(s)	POLG (1379)	Single gene sequencing >=10 amplicons

R315POLG相关疾病

检测标准

临床特征提示POLG相关疾病(包括癫痫持续状态及其他伴有其他提示性特征的严重难治性癫痫)

重叠指征

- 若临床特征不强烈提示POLG相关疾病且正在考虑更广泛的鉴别诊断，则应改用R27儿童期疾病或其他相关更广泛的检测
  不强烈提示POLG相关疾病且正在考虑更广泛的鉴别诊断

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在代谢医学、神经病学、儿童神经病学或临床遗传学顾问评估后就诊时，或在有mtDNA耗竭或多个mtDNA缺失证据时

申请专科

- 临床遗传学
- 代谢医学
- 神经科

专科服务组

- 线粒体

相关检测

请注意，对于R315临床指征申请，将进行以下所有检测，除非临床表现和/或初始结果表明并非所有检测都是必要的

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R315.1	常见POLG靶向变异变异检测	单人	小变异	单一区间	常见POLG变异	靶向变异检测
R315.2	POLG单基因测序	单人	小变异	单基因	POLG（1379）	单基因测序 >=10扩增子

R316 Pyruvate dehydrogenase (PDH) deficiency

Testing Criteria

Clinical features and laboratory features strongly suggestive of pyruvate dehydrogenase deficiency

Overlapping indications

- R63 Possible mitochondrial disorder - nuclear genes test should be considered where a broader range of mitochondrial nuclear genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant in Metabolic Medicine, Neurology, Paediatric Neurology or Clinical Genetics, or following skin biopsy and biochemical PDH assay in fibroblasts

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R316.1	Pyruvate dehydrogenase PDH deficiency WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Pyruvate dehydrogenase (PDH) deficiency (531)	WES or Medium panel

R316丙酮酸脱氢酶(PDH)缺乏症

检测标准

临床特征和实验室特征强烈提示丙酮酸脱氢酶缺乏症

重叠指征

• R63 可能的线粒体疾病--当考虑更广泛的一系列
线粒体核基因可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在代谢医学、神经病学、儿童神经病学或临床遗传学顾问评估后就诊时，或在成纤维细胞皮肤活检和生化PDH测定后

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R316.1	丙酮酸 脱氢酶 PDH 缺乏症 WES或中检测板	单人	小变异， 拷贝数变异	基因检测板或 基因座	丙酮酸脱氢酶（PDH） 缺乏症（531）	WES或Medium 检测组合

R317 Mitochondrial liver disease, including transient infantile liver failure

Testing Criteria

Infants (aged <2 years) with acute liver failure of unknown aetiology, or individuals with liver dysfunction suspected to be related to mitochondrial dysfunction

Where in Pathway

At presentation following assessment by a Consultant in Hepatology or Paediatric Hepatology, or following liver/muscle biopsy with evidence of respiratory chain deficiency and/or mtDNA depletion

Requesting Specialties

- Clinical Genetics
- Hepatology
- Metabolic Medicine

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R317.1	Mitochondrial liver disease Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Mitochondrial liver disease (532)	Small panel

R317线粒体肝脏疾病，包括暂时性婴儿肝脏衰竭

检测标准

病因不明的急性肝衰竭婴儿(年龄<2岁),或怀疑肝功能异常与线粒体功能障碍相关的个体

通路中的位置

在肝病学或儿童肝病学顾问评估后就诊时，或在肝脏/肌肉活检显示呼吸链缺陷和/或mtDNA耗竭证据后

申请专科

• 临床遗传学
• 肝脏病学
• 代谢医学

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R317.1	线粒体肝病 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	线粒体肝病(532) 小panel	

R350 MERRF syndrome

Testing Criteria

Clinical features suggestive of MERRF syndrome

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant in Metabolic Medicine, Neurology, Paediatric Neurology or Clinical Genetics

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R350.1	Common MERRF variants Targeted variant testing	Singleton	Small variants	Single interval	Common MERRF variants	Targeted variant testing

R350MERRF综合征

检测标准

提示MERRF综合征的临床特征

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在代谢医学、神经病学、儿童神经病学或临床遗传学顾问评估后就诊时

申请专科

• 临床遗传学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R350.1	常见MERRF靶向变异变异检测	单人	小变异	单一区间	常见MERRF变异	靶向变异检测

R351 NARP syndrome or maternally inherited Leigh syndrome

Testing Criteria

Clinical features suggestive of NARP syndrome (neuropathy, ataxia and retinitis pigmentosa) or MILS (maternally inherited Leigh syndrome)

Where in Pathway

At presentation following assessment by a Consultant in Metabolic Medicine, Neurology, Paediatric Neurology or Clinical Genetics

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology
- Ophthalmology

Specialist Service Group

- Mitochondrial

Associated Tests

Please note all the tests below will be undertaken for R351 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R351.1	MT-ATP6;	Singleton	Small variants	Small panel	MT-ATP6; (1368)	Single gene sequencing <10 amplicons
R351.2	m.8993T>C/G Targeted variant testing	Singleton	Small variants	Single interval	m.8993T>C/G	Targeted variant testing

R351NARP综合征或母系遗传Leigh综合征

检测标准

临床特征提示NARP综合征(神经病、共济失调和视网膜色素变性)或MILS(母系遗传Leigh综合征)

通路中的位置

在代谢医学、神经病学、儿童神经病学或临床遗传学顾问评估后就诊时

申请专科

- 临床遗传学
- 代谢医学
- 神经科
- 眼科

专科服务组

- 线粒体

相关检测

请注意，对于R351临床指征申请，将进行以下所有检测，除非临床表现和/或初始结果表明并非所有检测都是必要的

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R351.1	MT-ATP6；	单人	小变异	小检测板	MT-ATP6;(1368)	单基因测序 <10扩增子
R351.2	m.8993T>C/G靶向变异检测	单人	小变异	单一区间	m.8993T>C/G	靶向变异检测

R352 Mitochondrial DNA maintenance disorder

Testing Criteria

Clinical features suggestive of mtDNA maintenance disorder and/or evidence of mtDNA depletion or multiple mtDNA deletions

Overlapping indications

- R63 Possible mitochondrial disorder - nuclear genes test should be considered where a broader range of mitochondrial nuclear genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant in Metabolic Medicine, Neurology, Paediatric Neurology or Clinical Genetics, or following evidence of mtDNA depletion or multiple mtDNA deletions

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R352.1	Mitochondrial DNA maintenance disorder WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Mitochondrial DNA maintenance disorder (533)	WES or Medium Panel

R352线粒体DNA维持障碍

检测标准

临床特征提示mtDNA维持障碍和/或mtDNA耗竭或多个mtDNA缺失的证据

重叠指征

• R63 可能的线粒体疾病--当考虑更广泛的一系列
线粒体核基因可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在代谢医学、神经病学、儿童神经病学或临床遗传学顾问评估后就诊时，或在有mtDNA耗竭或多个mtDNA缺失证据时

申请专科

• 临床遗传学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R352.1	线粒体DNA维持疾病 WES或中检测	单人	小变异，拷贝数变异	基因检测板或基因座	线粒体DNA维持障碍（533）	WES或Medium检测板

R353 Mitochondrial disorder with complex I deficiency

Testing Criteria

Clinical features and laboratory features strongly suggestive of mitochondrial complex I deficiency

Overlapping indications

- R63 Possible mitochondrial disorder - nuclear genes test should be considered where a broader range of mitochondrial nuclear genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R353.1	Mitochondrial disorder with complex I deficiency WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Mitochondrial disorder with complex I deficiency (534)	WES or Medium Panel

R353线粒体疾病伴复合物I缺乏

检测标准

临床特征和实验室特征强烈提示线粒体复合物I缺乏症

重叠指征

• R63 可能的线粒体疾病--当考虑更广泛的一系列
线粒体核基因可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R353.1	线粒体伴障碍复合物 I缺陷 WES 或中等 p	单人	小变异，拷贝数变异	基因检测板或基因座	伴线粒体病复合体I缺乏症（534）	WES或Medium检测板

R354 Mitochondrial disorder with complex II deficiency

Testing Criteria

Clinical features and laboratory features strongly suggestive of mitochondrial complex II deficiency

Overlapping indications

- R63 Possible mitochondrial disorder - nuclear genes test should be considered where a broader range of mitochondrial nuclear genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R354.1	Mitochondrial disorder with complex II deficiency WES or small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Mitochondrial disorder with complex II deficiency (535)	WES or Small Panel

R354线粒体疾病伴复合物II缺乏

检测标准

临床特征和实验室特征强烈提示线粒体复合物II缺乏症

重叠指征

• R63 可能的线粒体疾病--当考虑更广泛的一系列
线粒体核基因可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R354.1	线粒体伴障碍复合物 II缺陷 WES 或小 par	单人	小变异，拷贝数变异	基因检测板或基因座	伴线粒体病复合物II缺乏症 (535)	WES或Small检测板

R355 Mitochondrial disorder with complex III deficiency

Testing Criteria

Clinical features and laboratory features strongly suggestive of mitochondrial complex III deficiency

Overlapping indications

- R63 Possible mitochondrial disorder - nuclear genes test should be considered where a broader range of mitochondrial nuclear genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R355.1	Mitochondrial disorder with complex III deficiency WES or small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Mitochondrial disorder with complex III deficiency (536)	WES or Small Panel

R355线粒体疾病伴复合物III缺乏

检测标准

临床特征和实验室特征强烈提示线粒体复合物III缺乏症

重叠指征

• R63 可能的线粒体疾病--当考虑更广泛的一系列
线粒体核基因可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R355.1	线粒体伴障碍复合物 III缺陷 WES 或小 par	单人	小变异，拷贝数变异	基因检测板或基因座	伴线粒体病复合物III缺乏症 (536)	WES或Small检测板

R356 Mitochondrial disorder with complex IV deficiency

Testing Criteria

Clinical features and laboratory features strongly suggestive of mitochondrial complex IV deficiency

Overlapping indications

- R63 Possible mitochondrial disorder - nuclear genes test should be considered where a broader range of mitochondrial nuclear genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R356.1	Mitochondrial disorder with complex IV deficiency	Singleton	Small variants, CNVs	Panel of genes or loci	Mitochondrial disorder with complex IV deficiency (537)	WES or Medium Panel

R356线粒体疾病伴复合物IV缺乏

检测标准

临床特征和实验室特征强烈提示线粒体复合物IV缺乏症

重叠指征

• R63 可能的线粒体疾病--当考虑更广泛的一系列
线粒体核基因可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R356.1	线粒体伴障碍复合物 IV缺乏症	单人	小变异，拷贝数变异	基因检测板或基因座	伴线粒体病复合物IV缺乏症 (537)	WES或Medium检测板

R357 Mitochondrial disorder with complex V deficiency

Testing Criteria

Clinical features and laboratory features strongly suggestive of mitochondrial complex V deficiency

Overlapping indications

- R63 Possible mitochondrial disorder - nuclear genes test should be considered where a broader range of mitochondrial nuclear genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R357.1	Mitochondrial disorder with complex V deficiency WES or small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Mitochondrial disorder with complex V deficiency (538)	WES or Small Panel

R357线粒体疾病伴复合物V缺乏

检测标准

临床特征和实验室特征强烈提示线粒体复合物V缺乏症

重叠指征

• R63 可能的线粒体疾病--当考虑更广泛的一系列
线粒体核基因可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R357.1	线粒体伴障碍复合体 V缺陷 WES 或小 par	单人	小变异，拷贝数变异	基因检测板或基因座	伴线粒体病复合物V缺乏症 (538)	WES或Small检测板

R63 Possible mitochondrial disorder - nuclear genes

Testing Criteria

Individuals with clinical features suggestive of a mitochondrial disorder requiring examination of nuclear genes where more targeted testing is not possible.

Overlapping indications

- Examination of the mitochondrial genome using one or more of the following indications should be considered first where possible based on clinical or biochemical/enzyme results:
  a. R42 Leber hereditary optic neuropathy
  b. R64 MELAS or MIDD
  c. R350 MERRF syndrome
  d. R351 NARP syndrome or maternally inherited Leigh syndrome
  e. R317 Mitochondrial liver disease, including transient infantile liver failure
  f. R299 Possible mitochondrial disorder - mitochondrial DNA rearrangement testing
  g. R300 Possible mitochondrial disorder - whole mitochondrial genome sequencing
  h. R301 Possible mitochondrial disorder - mitochondrial DNA depletion testing
- Targeted examination of nuclear genes should be considered first where possible based on clinical or biochemical/enzyme results:
  i. R315 POLG-related disorder
  j. R352 Mitochondrial DNA maintenance disorder
  k. R353 Mitochondrial disorder with complex I deficiency
  l. R354 Mitochondrial disorder with complex II deficiency
  m. R355 Mitochondrial disorder with complex III deficiency
  n. R356 Mitochondrial disorder with complex IV deficiency
  o. R356 Mitochondrial disorder with complex V deficiency
  p. R316 Pyruvate dehydrogenase (PDH) deficiency

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following assessment by a Consultant in Metabolic Medicine, Neurology, Paediatric Neurology or Clinical Genetics

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R63.1	Possible mitochondrial disorder - nuclear genes WES or large panel	Singleton	Small variants, CNVs	Panel of genes or loci	Possible mitochondrial disorder - nuclear genes (539)	WES or Large Panel

R63可能的线粒体疾病-核基因

检测标准

具有提示线粒体疾病的临床特征、需要检查核基因且无法进行更有针对性检测的个体。

重叠指征

• 使用以下一项或多项指征对线粒体基因组进行检查应
在可能的情况下，首先根据临床或生化/酶学结果考虑：
  a. R42 Leber遗传性视神经病变
  b. R64 MELAS或MIDD
  c. R350 MERRF综合征
  d. R351 NARP综合征或母系遗传Leigh综合征
  e. R317 线粒体肝病，包括婴儿暂时性肝衰竭
  f. R299 可能的线粒体疾病--线粒体DNA重排检测
  g. R300 疑似线粒体疾病--全线粒体基因组测序
  h. R301 可能的线粒体疾病--线粒体DNA耗竭检测
• 在可能的情况下，应首先考虑基于临床或
生化/酶学结果：
  i. R315 POLG相关疾病
  j. R352 线粒体DNA维持障碍
  k. R353 线粒体病伴复合体I缺乏症
  l. R354 线粒体复合物II缺乏症
  m. R355 线粒体复合物III缺乏症
  n. R356 线粒体疾病伴复合物IV缺乏
  o. R356 复合体V缺乏所致线粒体病
  p. R316 丙酮酸脱氢酶(PDH)缺乏症

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

经代谢医学、神经病学、儿童神经病学或临床遗传学顾问评估后

申请专科

• 临床遗传学
• 代谢医学
• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R63.1	可能的线粒体疾病 - 核基因 WES 或大 panel	单人	小变异，拷贝数变异	基因检测板或基因座	可能的线粒体疾病 - 核基因 (539)	WES或Large检测板

R394 Mitochondrial neurogastrointestinal encephalopathy

Testing Criteria

Clinical features suggestive of mitochondrial neurogastrointestinal encephalopathy (MNGIE) with elevated thymidine and deoxyuridine levels in blood and/or urine

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R394.1	TYMP Single gene sequencing	Singleton	Small variants	Single gene(s)	TYMP (1357)	Single gene sequencing >=10 amplicons

R394线粒体神经胃肠脑病

检测标准

具有提示线粒体神经胃肠脑病(MNGIE)的临床特征，伴血液和/或尿液中胸苷和脱氧尿苷水平升高

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 临床遗传学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R394.1	TYMP单基因测序	单人	小变异	单基因	TYMP (1357)	单基因测序 >=10扩增子

R395 Thiamine metabolism dysfunction syndrome 2

Testing Criteria

Clinical features and characteristic brain MRI changes suggestive of thiamine metabolism dysfunction syndrome 2 (also known as Biotin-responsive basal ganglia disease / thiamine responsive encephalopathy)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R395.1	SLC19A3 Single gene sequencing	Singleton	Small variants	Single gene(s)	SLC19A3 (1399)	Single gene sequencing <10 amplicons

R395硫胺素代谢功能障碍综合征2

检测标准

具有提示硫胺素代谢功能障碍综合征2(又称生物素反应性基底节病/硫胺素反应性脑病)的临床特征和特征性脑MRI改变。检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 临床遗传学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R395.1	SLC19A3单基因测序	单人	小变异	单基因	SLC19A3 (1399)	单基因测序 <10扩增子

R396 Mitochondrial Complex V deficiency, TMEM70 type

Testing Criteria

Infantile/paediatric onset hypertrophic cardiomyopathy, raised lactate and raised 3-methylglutaconic acid

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Cardiology
- Clinical Genetics
- Neurology

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R396.1	TMEM70 Single gene sequencing	Singleton	Small variants	Single gene(s)	TMEM70 (1356)	Single gene sequencing <10 amplicons

R396线粒体复合物V缺乏症，TMEM70型

检测标准

婴儿期/儿童期起病的肥厚型心肌病，乳酸升高和3-甲基戊烯二酸升高。检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 心脏病学

• 临床遗传学

• 神经科

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R396.1	TMEM70单基因测序	单人	小变异	单基因	TMEM70 (1356)	单基因测序 <10扩增子

R397 Maternally inherited cardiomyopathy

Testing Criteria

Maternally inherited hypertrophic cardiomyopathy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following laboratory or clinical assessment by a mitochondrial highly specialised service

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Mitochondrial

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R397.1	m.4300A>G Targeted variant testing	Singleton	Small variants	Single interval	m.4300A>G	Targeted variant testing

R397母系遗传心肌病

检测标准

母系遗传性肥厚型心肌病

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在经线粒体高度专业化服务进行实验室或临床评估后

申请专科

• 心脏病学

• 临床遗传学

专科服务组

• 线粒体

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R397.1	m.4300A>G 靶向变异检测	单人	小变异	单一区间	m.4300A>G	靶向变异检测

R42 Leber hereditary optic neuropathy

Testing Criteria

Likely or possible clinical diagnosis of Leber hereditary optic neuropathy

Where in Pathway

At presentation following assessment by a Consultant Ophthalmologist, Neurologist or Clinical Geneticist

Requesting Specialties

- Clinical Genetics
- Neurology
- Ophthalmology

Specialist Service Group

- Mitochondrial

Associated Tests

Please note all the tests below will be undertaken for R42 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R42.1	Three common LHON variants Targeted variant testing	Singleton	Small variants	Single interval	Three common LHON variants	Targeted variant testing
R42.2	Mitochondrial genome Whole mitochondrial genome sequencing	Singleton	Small variants	Mitochondrial Genome	Mitochondrial Genome	Mitochondrial Genome

R42Leber遗传性视神经病

检测标准

Leber遗传性视神经病变的疑似或可能临床诊断

通路中的位置

由眼科顾问医师、神经科医师或临床遗传学家评估后就诊时

申请专科

- 临床遗传学
- 神经科
- 眼科

专科服务组

- 线粒体

相关检测

请注意，对于R42临床指征请求，将进行以下所有检测，除非临床表现和/或初步结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R42.1	三种常见 LHON变异 靶向变异 检测	单人	小变异	单一区间	三种常见LHON变异	靶向变异 检测
R42.2	线粒体 全基因组 线粒体 基因组 测序	单人	小变异	线粒体 基因组	线粒体基因组	线粒体 基因组

Part XV. Mosaic and structural chromosomal disorders

R463 Cytogenetic characterisation of a genomic abnormality – Karyotype or Targeted Chromosome Analysis

Testing Criteria

Proband with possible structural chromosomal rearrangement requiring karyotype or targeted chromosome analysis (TCA), such as Robertsonian translocation, reciprocal translocation, ring chromosome, or other microscopically visible structural rearrangement, either indicated by, or alongside, findings from aneuploidy testing, microarray, WGS or other laboratory techniques. [TCA/Karyotype as appropriate]

NB: Application of either karyotype or TCA will be directed by professional judgement, best practice recommendation, clinical context and/or the type of cytogenetic rearrangement(s) detected. Due to the nature of cytogenetic analysis, reportable cytogenetic incidental findings may be detected during TCA.

Where in Pathway

At presentation or as indicated by previous testing

Requesting Specialties

- Clinical Genetics
- Genomics laboratory
- Fetal Medicine
- Endocrinology
- Paediatrics

Specialist Service Group

Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R463.1	Cytogenetic characterisation of a genomic abnormality – Karyotype or Targeted Chromosome Analysis	Singleton	copy number variant detection to genomewide resolution and structural variants or TCA	Genomewide or TCA	As determined by indication	Karyotype/TCA

第部分XV.嵌合及结构染色体疾病

R463细胞遗传学特征描述的一个基因组异常-核型分析或靶向染色体分析

检测标准

先证者可能存在需要核型分析或靶向染色体分析(TCA)的结构性染色体重排，如罗伯逊易位、相互易位、环状染色体或其他显微镜下可见的结构性重排，由非整倍体检测、微阵列(基因芯片)、WGS或其他实验室技术的发现所提示或与之同时存在。[酌情进行TCA/核型分析]

注：核型分析或TCA的应用将由专业判断、最佳实践建议、临床背景和/或所检测到的细胞遗传学重排类型决定。由于细胞遗传学分析的性质，在TCA过程中可能检测到可报告的细胞遗传学偶然发现。

通路中的位置

就诊时或根据既往检测结果所示

申请专科

- 临床遗传学
- 基因组实验室
- 胎儿医学
- 内分泌学
- 儿科

专科服务组

核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R463.1	细胞遗传学特征描述一个基因组异常－核型分析或靶向染色体分析	单人	拷贝数变异检测至全基因组范围分辨率及结构变异或TCA	全基因组范围或TCA	根据适应症确定	核型分析/TCA

R464 Recurrent miscarriage, products of conception not available – parental karyotype

Testing Criteria

. Recurrent miscarriage (defined as three or more miscarriages):

• where testing of the pregnancy loss has not been possible due to an unsuitable/failed sample e.g. no fetal material/MCC/fixed in formalin, and no previous losses have been successfully tested and reported. *Note that although parental karyotype analysis is available following a failed test, this is of limited utility and the most informative pathway is to test any subsequent pregnancy loss.*

Recurrent miscarriage (five or more pregnancy losses):

• Where none of the previous losses have been successfully tested and reported e.g. biochemical pregnancies, no products available for testing

Where in Pathway

At presentation

Requesting Specialties

- Clinical genetics
- Genomics Laboratory
- Fetal Medicine
- Pathology
- Gynaecology

Specialist Service Group

Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R464.1	Recurrent miscarriage – karyotype	Singleton	copy number variant detection to genomewide resolution and structural variants	Genomewide	As determined by indication	Karyotype

R464复发性流产，妊娠产物的受孕产物不可获得-父母核型

检测标准

.复发性流产(定义为三次或以上流产):• 当因样本不适宜/失败(例如无胎儿物质/MCC/福尔马林固定)而无法对妊娠丢失进行检测，且既往无流产成功检测并报告时。请注意，尽管检测失败后可进行父母核型分析，但其效用有限，最具信息量的路径是检测任何后续的妊娠丢失。复发性流产(五次或以上妊娠丢失):

• 既往流产均未成功检测和报告，例如生化妊娠，无可供检测的产物

通路中的位置

申请专科

• 临床遗传学
• 基因组实验室
• 胎儿医学
• 病理学
• 妇科

专科服务组

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R464.1	复发性流产 – 核型分析	单人	拷贝数变异检测至全基因组范围分辨率和结构变异	全基因组范围	根据适应症确定	核型分析

R465 Familial cytogenetic rearrangement - Karyotype or Targeted Chromosome Analysis

Testing Criteria

Cascade testing for known chromosomal rearrangement or family follow-up for possible balanced chromosomal rearrangement. [TCA/Karyotype as appropriate].

NB: Application of either karyotype or TCA will be directed by professional judgement, best practice recommendation, clinical context and/or the type of cytogenetic rearrangement(s) detected. Due to the nature of cytogenetic analysis, reportable cytogenetic incidental findings may be detected during TCA.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Genomics laboratory
- Fetal Medicine
- Endocrinology
- Paediatrics

Specialist Service Group

Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R465.1	Familial cytogenetic rearrangement - Karyotype or Targeted Chromosome Analysis	Singleton	copy number variant detection to genomewide resolution and structural variants or TCA	Genomewide or TCA	As determined by indication	Karyotype/TCA

R465家族性细胞遗传学重排-核型分析或靶向染色体分析

检测标准

针对已知染色体重排的级联检测或针对可能平衡染色体重排的家族随访。[酌情进行TCA/核型分析]。

注：核型分析或TCA的应用将由专业判断、最佳实践建议、临床背景和/或所检测到的细胞遗传学重排类型决定。由于细胞遗传学分析的性质，在TCA过程中可能检测到可报告的细胞遗传学偶然发现。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 基因组实验室
- 胎儿医学
- 内分泌学
- 儿科

专科服务组

核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R465.1	家族性细胞遗传学重排 - 核型分析或靶向染色体分析	单人	拷贝数变异检测至全基因组范围分辨率及结构variants或 TCA	全基因组范围或TCA	根据适应症确定	核型分析/TCA

R466 Unexplained infertility - karyotype

Testing Criteria

Unexplained infertility prior to infertility treatment

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Genomics laboratory
- Endocrinology
- Gynaecology
- Reproductive medicine

Specialist Service Group

Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R466.1	Unexplained infertility - karyotype	Singleton	copy number variant detection to genomewide resolution and structural variants	Genomewide	As determined by indication	Karyotype

R466不明原因不孕-核型分析

检测标准

不孕症治疗前的不明原因不孕症

通路中的位置

就诊时

申请专科

- 临床遗传学
- 基因组实验室
- 内分泌学
- 妇科
- 生殖医学

专科服务组

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R466.1	不明原因 不孕症 - 核型	单人	拷贝数 变异 全基因组范围 结构 变异 检测至 分辨率和	全基因组范围	根据适应症确定	核型分析

R467 Gamete donors - karyotype

Testing Criteria

Egg/sperm donor requiring a karyotype prior to acceptance

Where in Pathway

Where IVF centres with HFEA license are performing treatment with egg or sperm donation.

Requesting Specialties

Fertility Centres

Specialist Service Group

Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R467.1	Gamete donors	Singleton	Chromosome imbalance and/or structural variant	Genomewide		Karyotype

R467配子捐献者-核型分析

检测标准

需要在进行核型分析之前接受卵子/精子捐赠者

通路中的位置

持有HFEA许可证的IVF中心使用卵子或精子捐献进行治疗时。

申请专科

生育中心

专科服务组

核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R467.1	配子捐赠者	单人	染色体失衡和/或结构变异	全基因组范围		核型分析

R468 Possible sex chromosome aneuploidy or structural rearrangement – Targeted Chromosome Analysis

Testing Criteria

Clinical suspicion of a sex chromosome abnormality e.g. Turner syndrome, sex chromosome mosaicism, sex chromosome structural abnormality [TCA].

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Genomics Laboratory
- Endocrinology
- Paediatrics

Specialist Service Group

Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R468.1	Possible sex chromosome aneuploidy or structural rearrangement	Singleton	Chromosome imbalance and/or structural variant	Genomewide		TCA

R468可能的性染色体非整倍体或结构重排 -靶向染色体分析

检测标准

临床怀疑性染色体异常，例如Turner综合征、性染色体嵌合现象、性染色体结构异常[TCA]。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 基因组实验室
- 内分泌学
- 儿科

专科服务组

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R468.1	可能的性别染色体非整倍体或结构重排	单人	染色体失衡和/或结构变异	全基因组范围		TCA

R298 Possible structural or mosaic chromosomal abnormality - FISH

Testing Criteria

Possible structural or mosaic chromosomal abnormality requiring FISH

Testing for Y chromosome microdeletions should not routinely be performed before ICSI https://www.nice.org.uk/guidance/cg156/chapter/Recommendations

Overlapping indications

- R26 Likely common aneuploidy, test should be used for common aneuploidy testing, which may be delivered by FISH
- R463 Cytogenetic characterisation of a genomic abnormality – Karyotype or Targeted Chromosome Analysis
- R465 Familial cytogenetic rearrangement - Karyotype or Targeted Chromosome Analysis
- R265 Chromosomal mosaicism – karyotype, is available where extended karyotype is required
- R411 Y chromosome microdeletions is available where surgical sperm retrieval is considered

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following discussion with laboratory

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R298.1	Specific target FISH	Singleton	Balanced rearrangements	Single interval	As determined by indication	FISH

R298可能的结构或嵌合染色体异常-FISH

检测标准

可能需要FISH检测的结构性或嵌合型染色体异常

行Y染色体微缺失检测https://www.nice.org.uk/guidance/cg156/chapter/Recommendations

重叠指征

• R26 可能为常见非整倍体，应使用该检测进行常见非整倍体检测，可通过FISH实施

• R463 基因组异常的细胞遗传学特征描述 - 核型分析或靶向染色体分析
• R465 家族性细胞遗传学重排 - 核型分析或靶向染色体分析
• R265 染色体嵌合现象 - 核型分析，在需要扩展核型分析时可用
• R411 Y染色体微缺失，在考虑手术取精时可用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

与实验室讨论后

申请专科

• 临床遗传学
• 基因组实验室

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R298.1	特定靶标FISH单项检测		平衡的重排	单一区间	根据适应症确定	FISH

R265 Chromosomal mosaicism – karyotype / Targeted Chromosome Analysis

Testing Criteria

Individuals with possible mosaic chromosome abnormality requiring extended count karyotype including:

1. possible mosaic chromosome abnormality indicated by findings from conventional karyotype, microarray, WGS or other laboratory technique, OR
2. clinical features strongly suggestive of a specific chromosomal phenotype, for example Down syndrome, in whom conventional testing is negative

To note: Application of either karyotype or Targeted Chromosome Analysis (TCA) will be directed by professional judgement, best practice recommendation, clinical context and/or the type of cytogenetic rearrangement(s) detected. Due to the nature of cytogenetic analysis, reportable cytogenetic incidental findings may be detected during TCA.

Overlapping indications

- R343 Chromosomal mosaicism - microarray should be used where a microarray is indicated

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

N/A

Requesting Specialties

- Clinical Genetics
- Dermatology
- Genomics laboratory

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R265.1	Chromosomal mosaicism	Singleton	Aneuploidy	Genomewide	Genomewide	Karyotype / TCA

R265染色体嵌合现象-核型分析/靶向染色体分析

检测标准

可能存在嵌合染色体异常、需要扩展计数核型分析的个体，包括：1. 常规核型分析发现提示可能的嵌合染色体异常，微阵列(基因芯片)、WGS或其他实验室技术，或 2. 临床特征强烈提示特定染色体表型，例如Down综合征，常规检测阴性者

注意： 采用核型分析或靶向染色体分析(TCA)将由专业判断、最佳实践建议、临床背景和/或所检测到的细胞遗传学重排类型决定。由于细胞遗传学分析的性质，在TCA过程中可能检测到可报告的细胞遗传学偶然发现。

重叠指征

• R343 染色体嵌合现象 - 在有微阵列(基因芯片)指征时应使用微阵列(基因芯片)

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 皮肤病学
• 基因组实验室

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R265.1	染色体嵌合现象	单人	非整倍体	全基因组范围	全基因组范围	核型分析 / TCA

R343 Chromosomal mosaicism - microarray

Testing Criteria

Hyper- or hypo- pigmentation following Blaschkos lines (Hypomelanosis of Ito), with associated abnormalities such as neurodevelopmental delay, seizures or asymmetry

Overlapping indications

- R327 Mosaic skin disorders – deep sequencing test should be used where the mosaicism is likely to be caused by a single gene

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

NOTE: Sample submitted for this test can be either a skin biopsy or a blood sample

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R343.1	Genomewide Microarray	Singleton	Genomewide CNVs	Genomewide	Genomewide	Microarray

R343染色体嵌合现象-微阵列(基因芯片)

检测标准

沿Blaschko线分布的高色素或低色素沉着(Ito色素减退症)，伴有相关异常如神经发育迟缓、癫痫发作或不对称

重叠指征

• R327 嵌合性皮肤疾病--在嵌合现象可能存在的情况下应使用深度测序检测
由单个基因引起

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

注：本检测提交的样本可以是皮肤活检或血液样本

通路中的位置

申请专科

• 临床遗传学

• 皮肤病学

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R343.1	全基因组范围 微阵列（基因芯片）	单人	全基因组范围 拷贝数变异	全基因组范围	全基因组范围	微阵列（基因芯片）

R411 Y Chromosome microdeletions

Testing Criteria

Patients with non-obstructive azoospermia or severe oligospermia where testicular sperm extraction (TESE)/microdissection TESE (mTESE) is considered and outcome of testing will inform eligibility for (m)TESE and success of sperm retrieval (https://www.england.nhs.uk/wp-content/uploads/2018/07/Surgical-sperm-retrieval-for-male-infertility.pdf)

Testing for Y chromosome microdeletions should not routinely be performed before ICSI (https://www.nice.org.uk/guidance/cg156/chapter/Recommendations)

Testing for this clinical indication is performed by designated GLHs on behalf of the national genomic testing network

Overlapping indications

- R298 - Possible structural or mosaic chromosomal abnormality requiring FISH

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following review by a urologist with an interest in infertility or specialist fertility MDT

Requesting Specialties

- Clinical Genetics
- Urology / gynaecology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R411.1	Y chromosome microdeletions	Singleton	CNVs to exon level	Single interval	Y chromosome AZF regions	Targeted variant testing or equivalent

R411Y染色体微缺失

检测标准

非梗阻性无精子症或严重少精子症患者，在考虑睾丸精子提取(TESE)/显微切割睾丸精子提取(mTESE)且检测结果将影响(m)TESE资格及精子获取成功率时(https://www.england.nhs.uk/wp-content/uploads/2018/07/Surgical-男性不育的取精术.pdf)

不应在ICSI前常规进行Y染色体微缺失检测(https://www.nice.org.uk/guidance/cg156/chapter/Recommendations)

本临床指征的检测由指定的GLH代表国家基因组检测网络执行

重叠指征

• R298 - 可能需要 FISH 的结构性或嵌合型染色体异常

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

经对不孕症有兴趣的泌尿科医生或专科生育MDT审核后

申请专科

• 临床遗传学

• 泌尿科/妇科

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R411.1	Y染色体微缺失	单人	外显子CNVs水平	单一区间	Y染色体AZF区域	靶向变异检测或等效

Part XVI. Musculoskeletal

R52 Short stature - SHOX deficiency

Testing Criteria

Disproportionate short stature with features in the patient or relatives suggestive of SHOX deficiency, e.g. Madelung deformity,

Overlapping indications

- R382 Hypochondroplasia and R24 Achondroplasia
- R104 Skeletal dysplasia to be used where clinical features indicative of a likely monogenic skeletal dysplasia

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Paediatrics

Specialist Service Group

- Musculoskeletal

Associated Tests

Please note all the tests below will be undertaken for R52 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R52.1	SHOX MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	SHOX (1390)	MLPA or equivalent
R52.2	SHOX Single gene sequencing	Singleton	Small variants	Single gene(s)	SHOX (1390)	Single gene sequencing <10 amplicons

第XVI部分肌肉骨骼系统

R52矮身材-SHOX缺乏

检测标准

不成比例的身材矮小，患者或亲属具有提示SHOX缺乏的特征，例如Madelung畸形、

重叠指征

• R382 软骨发育不全症和 R24 软骨发育不全

• R104 骨骼发育不良检测，适用于临床特征提示可能为单基因骨骼发育不良

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 内分泌学

• 儿科

专科服务组

• 肌肉骨骼

相关检测

请注意，以下所有检测将针对R52临床指征申请进行，除非临床表现和/或初始结果表明并非所有检测都是必要的

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R52.1	SHOX MLPA或等效	单人	外显子水平拷贝数变异	单基因	SHOX (1390)	MLPA或等效
R52.2	SHOX单基因测序	单人	小变异	单基因	SHOX (1390)	单基因测序 <10扩增子

R24 Achondroplasia

Testing Criteria

Clinical features strongly suggestive of achondroplasia

Overlapping clinical indications:

- R309 NIPD for FGFR3-related skeletal dysplasias - variant testing
- R104 Skeletal dysplasia test should be used where features are atypical and a broader range of genes are likely to be causative
- R382 Hypochondroplasia testing may also be indicated if clinically relevant

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neonatology
- Paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R24.1	FGFR3 c.1138 Targeted variant testing	Singleton	Small variants	Single interval	FGFR3 c.1138	Targeted variant testing

R24软骨发育不全

检测标准

临床特征强烈提示软骨发育不全

重叠临床指征：

• R309 针对 FGFR3 相关骨骼发育不良的 NIPD--变异检测

• R104 骨骼发育不良检测应在特征不典型且需要更广泛基因范围时使用
可能具有致病性

• 如果具有临床相关性，R382 软骨发育不全检测也可能具有指征

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 新生儿科

• 儿科

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R24.1	FGFR3 c.1138 靶向变异检测	单人	小变异	单一区间	FGFR3 c.1138	靶向变异检测

R382 Hypochondroplasia

Testing Criteria

Clinical features strongly suggestive of hypochondroplasia

Overlapping clinical indications:

- R309 NIPD for FGFR3-related skeletal dysplasias - variant testing
- R24 Achondroplasia testing may also be indicated if clinically relevant
- R52 Short stature – SHOX deficiency
- R104 Skeletal dysplasia test should be used where features are atypical and a broader range of genes are likely to be causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Endocrinology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R382.1	FGFR3 c.1620 Targeted variant testing	Singleton	Small variants	Single interval	FGFR3 c.1620	Targeted variant testing

R382软骨发育不全

检测标准

临床特征强烈提示软骨发育低下重叠临床指征：

- R309 针对 FGFR3 相关骨骼发育不良的 NIPD--变异检测
- 如果具有临床相关性，R24 软骨发育不全检测也可能具有指征
- R52 身材矮小 - SHOX 缺陷
- R104 骨骼发育不良检测应在特征不典型且需要更广泛基因范围时使用
  可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 内分泌学

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R382.1	FGFR3 c.1620 靶向变异检测	单人	小变异	单一区间	FGFR3 c.1620	靶向变异检测

R25 Thanatophoric dysplasia

Testing Criteria

Clinical features strongly suggestive of thanatophoric dysplasia.

Overlapping clinical indications:

- R309 NIPD for FGFR3-related skeletal dysplasias - variant testing
- R104 Skeletal dysplasia test should be used where features are atypical and a broader range of genes are likely to be causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Fetal Medicine

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R25.1	FGFR3 Single gene sequencing	Singleton	Small variants	Single gene(s)	FGFR3 (1398)	Single gene sequencing >=10 amplicons

R25致死性发育不良

检测标准

临床特征强烈提示致死性发育不良。

重叠临床指征：

• R309 针对 FGFR3 相关骨骼发育不良的 NIPD--变异检测

• R104 骨骼发育不良检测应在特征不典型且更广泛的基因范围可能为致病原因时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 胎儿医学

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R25.1	FGFR3单基因测序	单人	小变异	单基因	FGFR3 (1398)	单基因测序 >=10扩增子

R104 Skeletal dysplasia

Testing Criteria

Clinical features indicative of a likely monogenic skeletal dysplasia.

Patients with suspected severe congenital autosomal recessive malignant osteopetrosis where rapid genetic diagnosis is required for urgent patient management (e.g. curative stem cell transplantation) are eligible for urgent testing via R104.4.

Isolated short stature, without evidence of an underlying abnormality of the bones is not appropriate to test via this indication. Please see overlapping indications for tests that may be more appropriate in these cases.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

R453 Monogenic short stature

R52 Short stature – SHOX deficiency

Where in Pathway

Following review of clinical features and x-rays by a Clinical Geneticist or Radiologist expert in skeletal dysplasias.

Requesting Specialties

- Clinical Genetics
- Paediatrics
- Endocrinology

Specialist Service Group

- Musculoskeletal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R104.3	Skeletal dysplasia WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Skeletal dysplasia (309)	WGS
R104.4	Osteopetrosis WES or large panel (urgent testing only)	Singleton	Small variants	Panel of genes or loci	Osteopetrosis (943)	WES or large panel

R104骨骼发育不良

检测标准

提示可能为单基因骨骼发育不良的临床特征。

疑似严重先天性常染色体隐性恶性骨硬化症且需要快速遗传学诊断以进行紧急患者管理(例如治愈性干细胞移植)的患者，有资格通过R104.4进行紧急检测。

孤立性身材矮小，无骨骼潜在异常证据者，不适合通过本指征进行检测。请参阅重叠指征以了解在这些情况下可能更合适的检测。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

R453 单基因性矮小症

R52 身材矮小 - SHOX 缺乏症

通路中的位置

经骨骼发育不良专家临床遗传学家或放射科医生审核临床特征和X线后。

申请专科

- 临床遗传学
- 儿科
- 内分泌学

专科服务组

- 肌肉骨骼

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R104.3	骨骼发育不良 WGS(第一阶段)	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	骨骼发育不良 (309)	全基因组测序
R104.4	骨硬化症 WES 或大检测板 (仅限紧急检测)	单人	小变异	基因检测板或基因座	骨硬化症 (943)	WES或大检测组合

R99 Common craniosynostosis syndromes

Testing Criteria

Recognisable multisuture craniosynostosis syndromes consistent with variants in EFNB1, ERF, FGFR1 common hot spots, FGFR2 common hot spots, FGFR3 common hot spots, TCF12 or TWIST1 or with unicoronal or bicoronal craniosynostosis

Overlapping indications

- R100 Rare syndromic craniosynostosis or isolated multisuture synostosis test should be used where features are not consistent with variants in EFNB1, ERF, FGFR1 common hot spots, FGFR2 common hot spots, FGFR3 common hot spots, TCF12 or TWIST1

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Musculoskeletal

Associated Tests

Please note all the tests below will be undertaken for R99 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R99.1	Common craniosynostosis syndromes Small panel	Singleton	Small variants	Panel of genes or loci	Common craniosynostosis syndromes (507)	Small panel
R99.2	Common craniosynostosis syndromes MLPA or equivalent	Singleton	Exon level CNVs	Panel of genes or loci	Common craniosynostosis syndromes (507)	MLPA or equivalent

R99常见颅缝早闭综合征

检测标准

可识别的多颅缝早闭综合征，与EFNB1、ERF、FGFR1常见热点、FGFR2常见热点、FGFR3常见热点、TCF12或TWIST1变异一致，或与单侧冠状缝或双侧冠状缝颅缝早闭一致

重叠指征

• R100 罕见综合征性颅缝早闭或孤立性多颅缝骨性融合检测应在以下情况下使用
特征与EFNB1、ERF、FGFR1常见热点、FGFR2常见热点、FGFR3常见热点、TCF12或TWIST1变异不一致

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

专科服务组

• 肌肉骨骼

相关检测

请注意，对于R99临床指征请求，将进行以下所有检测，除非临床表现和/或初步结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R99.1	常见颅缝早闭综合征小 panel	单人	小变异	基因检测板或基因座	常见颅缝早闭综合征 (507)	小检测板
R99.2	常见颅缝早闭综合征 MLPA 或等效方法	单人	外显子水平拷贝数变异	基因检测板或基因座	常见颅缝早闭综合征 (507)	MLPA或等效

R100 Rare syndromic craniosynostosis or isolated multisuture synostosis

Testing Criteria

Rare syndromic craniosynostosis syndrome or isolated multisuture synostosis, confirmed by skull scan where possible

Variants in EFNB1, ERF, FGFR1 common hot spots, FGFR2 common hot spots, FGFR3 common hot spots, TCF12 or TWIST1 must have been excluded on targeted genetic testing (R99 Common craniosynostosis syndromes)

Overlapping indications

- R99 Common craniosynostosis syndromes should be used where features are consistent with variants in EFNB1, ERF, FGFR1 common hot spots, FGFR2 common hot spots, FGFR3 common hot spots, TCF12 or TWIST1

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

NOTE: If the SMO gene is suspected as causative, a tissue sample will be required for testing

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Musculoskeletal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R100.3	Craniosynostosis WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Craniosynostosis (168)	WGS

R100罕见综合征性颅缝早闭或孤立性多颅缝骨性融合

检测标准

经颅骨扫描确认的罕见综合征性颅缝早闭综合征或孤立性多颅缝骨性融合

在可能的情况下

必须已通过靶向基因检测(R99 常见颅缝早闭综合征)排除EFNB1、ERF、FGFR1常见热点、FGFR2常见热点、FGFR3常见热点、TCF12或TWIST1变异

重叠指征

• R99 常见颅缝早闭综合征应在特征与EFNB1、ERF、FGFR1常见热点、FGFR2常见热点、FGFR3常见热点、TCF12或TWIST1变异一致时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

注：如怀疑SMO基因为致病原因，将需要组织样本进行检测

通路中的位置

申请专科

• 临床遗传学

专科服务组

• 肌肉骨骼

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R100.3	颅缝早闭 WGS(第一阶段)	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	颅缝早闭 (168)	全基因组测序

R416 Syndromic & non-syndromic craniosynostosis involving midline sutures

Testing Criteria

1. Patients presenting with confirmed craniosynostosis involving/including the metopic suture (trigonocephaly), OR

2. Sagittal suture, OR

3. both sagittal and metopic sutures.

Overlapping indications

- R100 Rare syndromic craniosynostosis or isolated multisuture synostosis

Where in Pathway

At presentation and following discussion with a consultant in clinical genetics or craniofacial neurosurgeon or another specialist approved by the GLH.

Requesting Specialties

- Clinical Genetics
- Neurosurgery

Specialist Service Group

- Musculoskeletal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R416.1	Syndromic & non-syndromic craniosynostosis involving midline sutures	Singleton	Small variant detection	Single gene(s)	SMAD6 (1395)	Single gene sequencing < 10 amplicons

R416综合征性&非综合征性颅缝早闭累及中线颅缝

检测标准

1. 表现为确诊的颅缝早闭，累及/包括额缝(三角头畸形)，或

2. 矢状缝，OR

3. 矢状缝和额缝。

重叠指征

• R100 罕见综合征性颅缝早闭或孤立性多颅缝早闭

通路中的位置

就诊时并经与临床遗传学顾问、颅面神经外科医生或GLH批准的其他专科医生讨论后。

申请专科

• 临床遗传学

• 神经外科

专科服务组

• 肌肉骨骼

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R416.1	综合征型与非综合征性颅缝早闭累及中线骨缝	单人	小变异检测	单基因	SMAD6 (1395)	单基因测序 < 10个扩增子

R340 Amelogenesis imperfecta

Testing Criteria

1. Significant developmental abnormalities of enamel quality and/or quantity affecting all or nearly all teeth of both dentitions (primary and secondary), AND
2. Environmental factors excluded

NOTE: Enamel abnormalities affecting unerupted permanent teeth can be detected on dental radiographs meaning that information about both dentitions is available well before eruption of the first permanent tooth

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following review by dentist expert in developmental dental disorders

Requesting Specialties

- Clinical Genetics
- Surgical Dentistry

Specialist Service Group

- Musculoskeletal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R340.1	Amelogenesis imperfecta WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Amelogenesis imperfecta (269)	WES or Medium panel

R340釉质发育不全

检测标准

1. 釉质质量 and/or 数量存在显著发育异常，影响全部或几乎所有牙齿两副牙列(乳牙列和恒牙列)均受累，且 2. 已排除环境因素

注：影响未萌出恒牙的釉质异常可通过牙科X线片检出，这意味着关于两副牙列的信息可在第一颗恒牙萌出前很久即已获得

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

经发育性牙科疾病专家牙医审核后申请专科

• 临床遗传学

• 口腔外科

专科服务组

• 肌肉骨骼

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R340.1	釉质形成 imperfecta WES或中等 Panel	单人	小变异，拷贝数变异	基因检测板或基因座	釉质发育不全 (269)	WES或Medium检测组合

R23 Apert syndrome

Testing Criteria

Clinical features strongly suggestive of Apert syndrome, including both craniosynostosis and syndactyly of the hands and feet, with or without additional features

Overlapping indications

- R306 NIPD for Apert syndrome - variant testing
- R99 Common craniosynostosis syndromes or R100 Rare syndromic craniosynostosis or isolated multisuture synostosis should be used where features are atypical and a broader range of genes are likely to be causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Musculoskeletal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R23.1	FGFR2 c.755 and c.758 Targeted variant testing	Singleton	Small variants	Single interval	FGFR2 c.755 and c.758	Targeted variant testing

R23Apert综合征

检测标准

临床特征强烈提示Apert综合征，包括颅缝早闭以及手和足并指(趾)，伴或不伴其他特征

重叠指征

- R306 用于Apert综合征的NIPD--变异检测
- R99 常见颅缝早闭综合征或R100 罕见综合征性颅缝早闭或孤立性多颅缝骨性融合应在特征不典型且可能涉及更广泛基因致病时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学

专科服务组

- 肌肉骨骼

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R23.1	FGFR2 c.755 和 c.758靶向变异检测	单人	小变异	单一区间	FGFR2 c.755和c.758	靶向变异检测

R101 Ehlers Danlos syndrome with a likely monogenic cause

Testing Criteria

Testing should only be used where it will impact on clinical management and cannot be used to exclude a diagnosis:

- Clinical features are indicative of one of the rare types of EDS (specified below), in particular hyperextensible skin, skin fragility with atrophic scarring, generalised tissue fragility with easy bruising and at unusual locations, rupture of vessels and/or hollow organs. Generalised joint hypermobility is common in the general population and will without other clinical features as mentioned above **not** be accepted for genetic testing.

The laboratory will discuss requests where the clinical indication is unclear with the national EDS service and will reject requests with insufficient information.

- Classical EDS (cEDS)
- Classical-like EDS (clEDS)
- Cardiac-valvular EDS (cvEDS)
- Vascular EDS (vEDS)
- Arthrochalasia EDS (aEDS)
- Dermatosparaxis EDS (dEDS)
- Kyphoscoliotic EDS (kEDS)
- Brittle Cornea Syndrome (BCS)
- Spondylodysplastic EDS (spEDS)
- Musculocontractural EDS (mcEDS)
- Myopathic EDS (mEDS)
- Periodontal EDS (pEDS)

Overlapping indications

- R89 Ultra-rare and atypical monogenic disorders or R27 Paediatric disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations not typical of disorders covered by the panel
- R125 Thoracic aortic aneurysm or dissection panel includes the COL1A1, COL3A1, COL5A1, COL5A2, PLOD1 and FKBP14 genes and may be a better option for patients presenting with aortic/arterial dilatation or rupture without additional features of EDS. Clarification may be sought from the highly specialised National Ehlers Danlos services: lnwh-tr.edslondonoffice@nhs.net or eds.sheffield@nhs.net .

Where in Pathway

Following assessment by a Clinical Geneticist or other expert in a highly specialised Ehlers Danlos service

Requesting Specialties

- Clinical Genetics
- Rheumatology

Specialist Service Group

- Musculoskeletal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R101.1	Ehlers Danlos syndromes WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Ehlers Danlos syndromes (53)	WES or Medium Panel

R101EhlersDanlos综合征伴可能单基因病因

检测标准

检测仅应在会影响临床管理时使用，且不能用于排除诊断：

• 临床特征提示EDS的某种罕见类型(详见下文)，特别是
皮肤过度伸展、皮肤脆弱伴萎缩性瘢痕、全身组织脆弱伴易瘀伤且位于不寻常部位、血管和/或空腔器官破裂。全身关节过度活动在一般人群中常见，若无上述其他临床特征，**不**会被接受进行基因检测。

实验室将与国家EDS服务中心讨论临床指征不明确的请求，并拒绝信息不足的请求。

• 经典型 EDS(cEDS)
• 经典型样 EDS(clEDS)
• 心脏瓣膜型 EDS(cvEDS)
• 血管型 EDS(vEDS)
• 关节松弛型 EDS(aEDS)
• 皮肤脆裂型埃勒斯-当洛斯综合征(dEDS)
• 脊柱后侧凸型 EDS(kEDS)
• 脆性角膜综合征(BCS)
• 脊椎发育不良型 EDS(spEDS)
• 肌肉挛缩型 EDS(mcEDS)
• 肌病型 EDS(mEDS)
• 牙周型 EDS(pEDS)

重叠指征

• R89 超罕见和非典型单基因疾病或R27 儿科疾病检测应在以下个体中使用
具有先天性畸形、畸形特征或其他复杂或综合征性表现，且非panel所涵盖疾病的典型表现

• R125 胸主动脉瘤或夹层panel包括COL1A1、COL3A1、COL5A1、COL5A2、PLOD1和FKBP14基因，对于表现为主动脉/动脉扩张或破裂而无其他EDS特征的患者可能是更好的选择。可向高度专业化的国家Ehlers Danlos服务中心寻求澄清：lnwh-tr.edslondonoffice@nhs.net 或 eds.sheffield@nhs.net。

通路中的位置

经临床遗传学家或高度专业化Ehlers Danlos服务中心的其他专家评估后

申请专科

• 临床遗传学
• 风湿病学

专科服务组

• 肌肉骨骼

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R101.1	埃勒斯-当洛斯综合征 WES 或中通量面板	单人	小变异，拷贝数变异	基因检测板或基因座	埃勒斯-当洛斯综合征 (53)	WES或Medium检测板

R102 Osteogenesis imperfecta

Testing Criteria

Clinical features indicative of a likely monogenic bone fragility disorder / rare and atypical forms of osteogenesis imperfecta.

In adults, testing is only routinely recommended where it will impact on reproductive choices
Testing should only be used where it will impact on clinical management.

Referrals where non-accidental injury is suspected should be discussed with the OI Highly Specialised Service before requesting genomic testing.

Overlapping indications

- R89 Ultra-rare and atypical monogenic disorders or R27 Paediatric disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations not typical of disorders covered by the panel

Where in Pathway

Following assessment by a Clinical Geneticist or other expert in highly specialised osteogenesis imperfecta service

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Rheumatology
- Metabolic medicine

Specialist Service Group

- Musculoskeletal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R102.1	Osteogenesis imperfecta WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Osteogenesis imperfecta (196)	WES or Medium Panel

R102成骨不全

检测标准

提示可能为单基因骨脆性疾病的临床特征/罕见及非典型形式的成骨不全。

在成人中，仅常规推荐在检测将影响生育选择的情况下进行检测。检测仅应在将影响临床管理的情况下使用。

疑似非意外伤害的转诊应在申请基因组检测前与成骨不全高度专业化服务团队讨论。

重叠指征

• 对于具有先天性畸形、畸形特征或其他非该检测面板所涵盖疾病典型表现的复杂或综合征性表现的个体，应使用R89超罕见及非典型单基因疾病检测或R27儿科疾病检测

通路中的位置

经临床遗传学家或其他高度专业化成骨不全服务专家评估后

申请专科

• 临床遗传学
• 内分泌学
• 风湿病学
• 代谢医学

专科服务组

• 肌肉骨骼

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R102.1	成骨 imperfecta WES或中通量面板	单人	小变异，拷贝数变异	基因检测板或基因座	成骨不全 (196)	WES或Medium检测板

R390 Multiple exostoses

Testing Criteria

Individuals with multiple exostoses (osteochondromas) where a monogenic cause is likely and a molecular diagnosis will contribute to management or advice

Where in Pathway

At presentation or when a molecular diagnosis becomes necessary for management or advice

Requesting Specialties

- Clinical Genetics
- Orthopaedics
- Rheumatology

Specialist Service Group

- Musculoskeletal

Associated Tests

Please note all the tests below will be undertaken for R390 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R390.1	EXT1; EXT2	Singleton	Small variants	Small panel	EXT1; EXT2 (1367)	Small panel
R390.2	EXT1; EXT2 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	EXT1; EXT2 (1367)	MLPA or equivalent

R390多发性外生骨疣

检测标准

具有多发性外生骨疣(骨软骨瘤)且可能为单基因病因、分子诊断将有助于管理或建议的个体

通路中的位置

就诊时或当分子诊断对管理或建议变得必要时

申请专科

- 临床遗传学
- 骨科
- 风湿病学

专科服务组

- 肌肉骨骼

相关检测

请注意，对于R390临床指征申请，将进行以下所有检测，除非临床表现和/或初步结果表明并非所有检测都是必要的

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R390.1	EXT1；EXT2	单人	小变异	小检测板	EXT1；EXT2 (1367)	小检测板
R390.2	EXT1；EXT2 MLPA或等效方法	单人	外显子水平拷贝数变异	单基因	EXT1；EXT2 (1367)	MLPA或等效

Part XVII. Neurology

R70 Spinal muscular atrophy type 1 diagnostic test

Testing Criteria

Clinical features suggestive of spinal muscular atrophy type 1

NOTE: pre symptomatic testing of siblings of individuals with a molecularly confirmed diagnosis of SMA, where testing may inform treatment decisions, should use R242

Overlapping indications

- R69 Hypotonic infant with a likely central cause test should be used in floppy babies where the clinical picture is suggestive of a central cause, i.e. particularly where the baby is not alert, but lethargic or sleepy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neonatology
- Neurology
- Paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R70.1	SMN1, SMN2 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	SMN1; SMN2	MLPA or equivalent

第XVII部分神经病学

R70脊髓性肌萎缩1型诊断检测

检测标准

提示脊髓性肌萎缩症1型的临床特征

注：对于分子学确诊为SMA患者的同胞，若检测可能影响治疗决策，症状前检测应使用R242

重叠指征

• 对于临床情况提示中枢性病因的肌张力低下婴儿，应使用R69肌张力低下婴儿可能中枢性病因检测，即表现提示中枢性病因，即尤其是婴儿不警觉，而是昏睡或嗜睡时

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 新生儿科
• 神经科
• 儿科

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R70.1	SMN1、SMN2 MLPA或等效方法	单人	外显子水平拷贝数变异	单基因	SMN1；SMN2	MLPA或等效

R71 Spinal muscular atrophy type 1 rare variant testing

Testing Criteria

Individuals in whom a rare variant in the SMN1 gene is likely. This will mainly be used for individuals with clinical features of spinal muscular atrophy (SMA) type 1 and monoallelic copy number variant of SMN1

NOTE: pre symptomatic testing of siblings of individuals with a molecularly confirmed diagnosis of SMA, where testing may inform treatment decisions, should use R242

Overlapping indications

- R70 Spinal muscular atrophy type 1 diagnostic test should be used first where clinical features are suggestive of spinal muscular atrophy type 1 and SMN1 copy number has not been tested.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

After SMN1 copy number analysis

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R71.1	SMN1 Single gene sequencing	Singleton	Small variants	Single gene(s)	SMN1 (1393)	Single gene sequencing >=10 amplicons

R71脊髓性肌萎缩1型罕见变异检测

检测标准

可能携带SMN1基因罕见变异的个体。这主要用于具有脊髓性肌萎缩(SMA)1型临床特征和SMN1单等位基因拷贝数变异的个体

注：对于分子学确诊为SMA患者的同胞，若检测可能影响治疗决策，症状前检测应使用R242 重叠指征

- 当临床特征提示脊髓性肌萎缩1型且SMN1拷贝数尚未检测时，应首先使用R70脊髓性肌萎缩1型诊断检测。
  提示脊髓性肌萎缩1型且SMN1拷贝数尚未检测。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

SMN1拷贝数分析后

申请专科

- 临床遗传学
- 神经科

专科服务组

- 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R71.1	SMN1单基因测序	单人	小变异	单基因	SMN1 (1393)	单基因测序 >=10扩增子

R72 Myotonic dystrophy type 1

Testing Criteria

Clinical features strongly suggestive of myotonic dystrophy type 1

Overlapping indications

- R69 Hypotonic infant with a likely central cause test should be used in floppy babies where the clinical picture is suggestive of a central cause
- R381 Other rare neuromuscular disorders should be used where clinical features are atypical and a broader range of genes are potentially causative
- R410 Myotonic dystrophy type 2 should be used where there is clinical suspicion of myotonic dystrophy type 2 or where myotonic dystrophy type 1 has been excluded

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R72.1	DMPK STR testing	Singleton	Methylation	Single gene(s)	DMPK STR	STR testing

R72强直性营养不良1型

检测标准

临床表现高度提示1型强直性肌营养不良

重叠指征

- 对于临床情况提示中枢性病因的肌张力低下婴儿，应使用R69肌张力低下婴儿可能中枢性病因检测，即影像提示中枢性病因
- 当临床特征不典型且存在其他罕见神经肌肉疾病时，应使用R381其他罕见神经肌肉疾病更广泛的基因范围可能具有致病性
- 当临床怀疑强直性肌营养不良时，应使用R410强直性肌营养不良2型2型，或已排除1型强直性肌营养不良

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 神经科

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R72.1	DMPK短串联重复序列检测	单人	甲基化	单基因	DMPK STR	STR检测

R77 Hereditary neuropathy - PMP22 copy number

Testing Criteria

Hereditary neuropathy where PMP22 copy number abnormalities are possible

Overlapping indications

- R78 Hereditary neuropathy or pain disorder test should be used where PMP22 copy number abnormalities are clinically unlikely or have already been excluded
- R89 Ultra-rare and atypical monogenic disorders or R27 Paediatric disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology
- Paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R77.1	PMP22 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	PMP22	MLPA or equivalent

R77遗传性神经病-PMP22拷贝数

检测标准

遗传性神经病，可能存在PMP22拷贝数异常

重叠指征

• 当PMP22拷贝数时，应使用R78遗传性神经病或疼痛障碍检测
异常在临床上不太可能或已被排除

• R89 超罕见和非典型单基因疾病或R27 儿科疾病检测应在以下个体中使用
患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 临床遗传学

• 神经科

• 儿科

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R77.1	PMP22 MLPA或等效	单人	外显子水平拷贝数变异	单基因	PMP22	MLPA或等效

R68 Huntington disease

Testing Criteria

Clinical features that indicate a likely diagnosis of Huntington disease

- Specialties other than those listed in Requesting Specialties may request tests in certain settings following discussion with their local laboratory-clinical team

Overlapping indications

- R56 Adult onset dystonia, chorea or related movement disorder or other relevant broader test should be used where clinical features are not strongly suggestive of Huntington disease

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology
- Psychiatry

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R68.1	HTT STR testing	Singleton	STRs	Single gene(s)	HTT STR	STR testing

R68亨廷顿病

检测标准

提示可能诊断为亨廷顿病的临床特征

- 申请专科以外的其他专科可在某些情况下申请检测
  在与当地实验室-临床团队讨论后

重叠指征

- R56成人起病肌张力障碍、舞蹈症或相关运动障碍或其他相关更广泛检测应用于临床特征不强烈提示亨廷顿病的情况

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 神经科
- 精神病学

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R68.1	HTT短串联重复序列检测	单人	短串联重复序列	单基因	HTT STR	STR检测

R383 Linkage testing for Huntington disease

Testing Criteria

Families with a confirmed diagnosis of Huntington disease who require linkage testing to guide management or advice

Where in Pathway

As appropriate

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R383.1	HTT Linkage testing	Multiple affected individuals	Other	Single gene(s)	HTT	Other

R383连锁分析用于亨廷顿病

检测标准

确诊为亨廷顿病且需要连锁分析以指导管理或建议的家系

通路中的位置

酌情

申请专科

• 临床遗传学

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R383.1	HTT连锁检测	多个受累个体	其他	单基因	HTT	其他

R471 Neurodegenerative Disorders, adult onset – Prenatal Exclusion Testing

Testing Criteria

Families with a confirmed molecular diagnosis of an adult onset neurodegenerative disorder, with causative variants identified on one of the genes listed below, where linkage analysis is required for prenatal testing of a familial high risk haplotype.

For this test, samples are needed from the pregnant couple and from both grandparents on the affected side. For other family structures please contact the laboratory on a case by case basis.

Referral prior to pregnancy is essential so that all relevant family members can be tested to ensure the linkage will be informative before the testing is performed.

Prenatal exclusion testing is currently only available for the following causative loci;

- C9orf72
- SOD1
- MAPT
- PSEN1

Prenatal exclusion testing is also available for Huntington disease (HTT gene) but test directory code R383 Linkage testing for Huntington disease should be used

Overlapping indications

R383 Linkage testing for Huntington disease

Where in Pathway

As appropriate.

Requesting Specialties

- Clinical genetics

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R471.1	C9orf72 linkage testing	3 generations	Haplotyping	Single gene	C9orf72	Linkage
R471.2	SOD1 linkage testing	3 generations	Haplotyping	Single gene	SOD1	Linkage
R471.3	MAPT linkage testing	3 generations	Haplotyping	Single gene	MAPT	Linkage
R471.4	PSEN1 linkage testing	3 generations	Haplotyping	Single gene	PSEN1	Linkage

R471神经退行性疾病，成人起病-产前排除检测

检测标准

分子确诊为成人起病神经退行性疾病的家系，致病变异已在下列基因之一中识别，需要对家族高风险单倍型进行产前检测的连锁分析。

对于此检测，需要来自怀孕夫妇及受累方双方祖父母的样本。对于其他家庭结构，请逐案联系实验室。

妊娠前转诊至关重要，以便对所有相关家庭成员进行检测，确保在进行检测前连锁分析具有信息性。

目前产前排除检测仅适用于以下致病位点；

- C9orf72
- SOD1
- MAPT
- PSEN1

产前排除检测也适用于亨廷顿病(HTT 基因)，但应使用检测目录代码 R383 亨廷顿病连锁检测

重叠指征

R383 亨廷顿病连锁检测

通路中的位置

申请专科

- 临床遗传学

专科服务组

- 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R471.1	C9orf72连锁检测	3代单倍型分析 单基因			C9orf72	连锁
R471.2	SOD1关联检测	3代单倍型分析 单基因			SOD1	连锁
R471.3	MAPT连锁检测	3代单倍型分析 单基因			MAPT	连锁
R471.4	PSEN1连锁检测	3代单倍型分析 单基因			PSEN1	连锁

R252 SMA carrier testing at population risk for partners of known carriers

Testing Criteria

Testing in partners of known carriers of SMA where management of a current or future pregnancy depends on the result

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At the time of reproductive planning

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R252.1	SMN1 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	SMN1	MLPA or equivalent

R252SMA携带者检测在人群风险对于伴侣的已知携带者

检测标准

对已知 SMA 携带者的伴侣进行检测，当前或未来妊娠的管理取决于检测结果

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在生育计划时

申请专科

• 临床遗传学

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R252.1	SMN1 MLPA或等效	单人	外显子水平拷贝数变异	单基因	SMN1	MLPA或等效

R54 Hereditary ataxia with onset in adulthood

Testing Criteria

Unexplained ataxia with onset in adulthood including where differential diagnosis encompasses STR loci.

Overlapping indications

R60 Adult onset hereditary spastic paraplegia

Where in Pathway

At presentation following assessment by a Neurologist

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Please note R54.4 (RFC1 STR) will not be included unless specifically requested

From April 2026: The gene content of the Adult onset neurological disorders panel includes all genes on Hereditary ataxia with onset in adulthood (R54), Adult onset dystonia, chorea or related movement disorder (R56), Adult onset neurodegenerative disorders (previously R58, now R458, R459, R460 & R461), Adult onset hereditary spastic paraplegia (R60)

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R54.3	Hereditary ataxia - adult onset WGS (phase 1)	Trio or Singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Adult onset neurological disorders (1669)	WGS
R54.4	*RFC1* STR	Singleton	STRs	Panel of genes or loci	*RFC1* STR	STR testing

R54遗传性共济失调伴成年期发病

检测标准

不明原因的成年起病共济失调，包括鉴别诊断涵盖STR位点的情况。

重叠指征

R60 成人起病遗传性痉挛性截瘫

通路中的位置

就诊时经神经科医师评估后

申请专科

- 临床遗传学
- 神经科

专科服务组

- 神经科

相关检测

请注意，除非特别要求，否则不包含R54.4(RFC1 STR)

自2026年4月起：成人起病神经系统疾病 panel 的基因内容包含以下 panel 的全部基因：成人起病遗传性共济失调(R54)、成人起病肌张力障碍、舞蹈症或相关运动障碍(R56)、成人起病神经退行性疾病(原 R58，现为 R458、R459、R460 和 R461)、成人起病遗传性痉挛性截瘫(R60)

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R54.3	遗传性共济失调 - 成人起病全基因组测序（第一阶段）	三人组或单人	外显子水平 CNVs，小变异序列，短串联重复	基因组或基因座	成人起病神经系统疾病 (1669)	全基因组测序
R54.4	RFC1 短串联重复序列	单人	短串联重复序列	基因组或位点	RFC1 短串联重复序列	STR检测

R55 Hereditary ataxia with onset in childhood

Testing Criteria

Unexplained hereditary ataxia with onset in childhood including where differential diagnosis encompasses STR loci

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R55.4	Hereditary ataxia and cerebellar anomalies - childhood onset WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Hereditary ataxia and cerebellar anomalies - childhood onset (488)	WGS

R55遗传性共济失调伴儿童期起病

检测标准

不明原因的儿童期起病遗传性共济失调，包括鉴别诊断涵盖STR位点的情况

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经神经科医师评估后

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R55.4	遗传性共济失调和小脑异常 - 儿童期起病 WGS(第一阶段)	三人组或单人 外显子水平	CNVs，小变异，短串联重复	基因检测板或基因座	遗传性共济失调和小脑异常 - 儿童起病 (488)	全基因组测序

R56 Adult onset dystonia, chorea or related movement disorder

Testing Criteria

One of the following:

1. Unexplained isolated dystonia, chorea or related movement disorder with onset before age of 30, or familial
2. Unexplained complex dystonia, chorea or related movement disorder with onset before age of 45, or familial
3. HD-like (regardless of age or dystonia type), following a negative R68 HD test

Overlapping indications

- R68 Huntington disease test should be used where clinical features indicate a likely diagnosis of Huntington disease

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

From April 2026: The gene content of the Adult onset neurological disorders panel includes all genes on Hereditary ataxia with onset in adulthood (R54), Adult onset dystonia, chorea or related movement disorder (R56), Adult onset neurodegenerative disorders (previously R58, now R458, R459, R460 & R461), Adult onset hereditary spastic paraplegia (R60)

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R56.3	Adult onset dystonia, chorea, or related movement disorder WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Adult onset neurological disorders (1669)	WGS

R56成人起病肌张力障碍、舞蹈症或相关运动障碍

检测标准

以下之一：

1. 不明原因的孤立性肌张力障碍、舞蹈症或相关运动障碍，起病年龄在30岁之前，或有家族史
2. 不明原因的复杂性肌张力障碍、舞蹈症或相关运动障碍，起病年龄在45岁之前，或有家族史
3. 类亨廷顿病(无论年龄或肌张力障碍类型)，在R68亨廷顿病检测阴性后

重叠指征

• 当临床特征提示可能诊断为亨廷顿病时，应使用R68亨廷顿病检测
亨廷顿病

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经神经科医师评估后

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

自2026年4月起：成人起病神经系统疾病 panel 的基因内容包含以下 panel 的全部基因：成人起病遗传性共济失调(R54)、成人起病肌张力障碍、舞蹈症或相关运动障碍(R56)、成人起病神经退行性疾病(原 R58，现为 R458、R459、R460 和 R461)、成人起病遗传性痉挛性截瘫(R60)

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R56.3	成人起病肌张力障碍、舞蹈症、或相关运动疾病 WGS (phase 2)	三人组或单人 外显子水平	CNVs，小变异，短串联重复序列	基因检测板或基因座	成人起病神经系统疾病 (1669)	全基因组测序

R57 Childhood onset dystonia, chorea or related movement disorder

Testing Criteria

Unexplained dystonia, chorea or related movement disorder with onset in childhood with a likely monogenic cause

Overlapping indications

- R61 Childhood onset hereditary spastic paraplegia – if the patient has spastic paraplegia
- R55 Hereditary ataxia with onset in childhood – if the patient has ataxia
- R27 Paediatric disorders
- R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R57.5	Childhood onset dystonia or chorea or related movement disorder WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Childhood onset dystonia or chorea or related movement disorder (847)	WGS

R57儿童期起病肌张力障碍、舞蹈症或相关运动障碍

检测标准

不明原因的儿童期起病肌张力障碍、舞蹈症或相关运动障碍，具有可能的单基因病因

重叠指征

- R61儿童期起病遗传性痉挛性截瘫--若患者患有痉挛性截瘫
- R55 儿童期起病的遗传性共济失调--如果患者存在共济失调
- R27 儿科疾病
- R89超罕见及非典型单基因疾病检测应适用于具有复杂或综合征性表现

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经神经科医师评估后

申请专科

- 临床遗传学
- 代谢医学
- 神经科

专科服务组

- 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R57.5	儿童起病肌张力障碍或舞蹈症或相关运动疾病 WGS (phase 2)	三人组或单人 外显子水平	CNVs，小变异，短串联重复	基因检测板或基因座	儿童起病肌张力障碍或舞蹈症或相关运动障碍 (847)	全基因组测序

R458 Young onset or familial dementia

Testing Criteria

Unexplained dementia where acquired causes (e.g. stroke, tumour) have been excluded AND

a. Age at onset <55 years, OR
b. First or second degree relative with MND/ALS OR
c. Neurological features suggestive of a monogenic disorder where cognitive impairment is part of a wider phenotype, OR
d. Family history highly suggestive of a monogenic cause for dementia for example one or more first or second degree relatives with dementia onset <65y where the type of dementia is the same as the proband. **NOTE a family history of dementia of uncertain or mixed type where onset is predominantly over 65y is unlikely to represent a monogenic disorder.**

Where in Pathway

At presentation following assessment by a Neurologist

Requesting Specialties

- Clinical Genetics
- Neurology
- Psychiatry

Specialist Service Group

- Neurology

Associated Tests

From April 2026: The gene content of the Adult onset neurological disorders panel includes all genes on Hereditary ataxia with onset in adulthood (R54), Adult onset dystonia, chorea or related movement disorder (R56) Adult onset neurodegenerative disorders (previously R58, now R458, R459, R460 & R461), Adult onset hereditary spastic paraplegia (R60)

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R458.1	Young onset or familial dementia	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Adult onset neurological disorders (1669)	WGS

R458青年起病或家族性痴呆

检测标准

不明原因的痴呆，已排除获得性病因(如卒中、肿瘤)且

a. 发病年龄<55岁,或
b. 一级或二级亲属患有MND/ALS，或
c. 神经系统特征提示单基因疾病，且认知障碍是更广泛表型的一部分，或
d. 家族史高度提示痴呆的单基因病因，例如一名或多名一级或二级亲属痴呆起病<65岁,且痴呆类型与先证者相同。**注意：痴呆类型不确定或混合、起病年龄主要超过65岁的家族史不太可能代表单基因疾病。**

通路中的位置

就诊时经神经科医师评估后

申请专科

• 临床遗传学
• 神经科
• 精神病学

专科服务组

• 神经科

相关检测

自2026年4月起：成人起病神经系统疾病panel的基因内容包含以下所有基因：成人起病遗传性共济失调(R54)、成人起病肌张力障碍、舞蹈症或相关运动障碍(R56)、成人起病神经退行性疾病(原R58，现为R458、R459、R460及R461)、成人起病遗传性痉挛性截瘫(R60)

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R458.1	青年起病或家族性痴呆	三人组或单人	外显子水平CNVs，小变异，短串联重复序列	基因组或基因座	成人起病神经系统疾病 (1669)	全基因组测序

R459 Young onset or complex Parkinson disease

Testing Criteria

Parkinson's disease or complex Parkinsonism with a likely monogenic cause AND

a. Age at onset <50 years, OR
b. First degree relative affected at <50 years, OR
c. Complex features such as spasticity, gaze palsy, early dementia, early bulbar failure, dyspraxia, ataxia, postural hypotension, cortical sensory loss, iron accumulation on brain MRI.

Where in Pathway

At presentation following assessment by a Neurologist

Requesting Specialties

- Clinical Genetics
- Neurology
- Psychiatry

Specialist Service Group

- Neurology

Associated Tests

From April 2026: The gene content of the Adult onset neurological disorders panel includes all genes on Hereditary ataxia with onset in adulthood (R54), Adult onset dystonia, chorea or related movement disorder (R56) Adult onset neurodegenerative disorders (previously R58, now R458, R459, R460 & R461), Adult onset hereditary spastic paraplegia (R60)

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R459.1	Young onset or complex Parkinson disease	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Adult onset neurological disorders (1669)	WGS

R459青年起病或复杂型帕金森病

检测标准

帕金森病或可能由单基因病因导致的复杂帕金森综合征，且

a. 发病年龄<50岁,或
b. 一级亲属在<50岁时患病,或
c. 复杂特征，如痉挛、凝视麻痹、早期痴呆、早期延髓功能衰竭、运用障碍、共济失调、体位性低血压、皮质感觉丧失、脑MRI铁沉积。

通路中的位置

就诊时经神经科医师评估后

申请专科

• 临床遗传学
• 神经科
• 精神病学

专科服务组

• 神经科

相关检测

自2026年4月起：成人起病神经系统疾病panel的基因内容包含以下所有基因：成人起病遗传性共济失调(R54)、成人起病肌张力障碍、舞蹈症或相关运动障碍(R56)、成人起病神经退行性疾病(原R58，现为R458、R459、R460及R461)、成人起病遗传性痉挛性截瘫(R60)

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R459.1	早发型或复杂性帕金森病	三人组或单人	外显子水平CNVs，小变异，短串联重复序列	基因组或基因座	成人起病神经系统疾病 (1669)	全基因组测序

R460 Amyotrophic lateral sclerosis

Testing Criteria

Amyotrophic lateral sclerosis (ALS) with a likely monogenic cause, with or without frontotemporal dementia
AND:

a. Evidence of lower motor neuron (LMN) degeneration by clinical, electrophysiologic or neuropathologic examination, AND
b. Evidence of upper motor neuron (UMN) degeneration by clinical examination, AND
c. Progressive course, AND
e. No evidence of other aetiology

Where in Pathway

At presentation following assessment by a Neurologist

Requesting Specialties

- Clinical Genetics
- Neurology
- Psychiatry

Specialist Service Group

- Neurology

Associated Tests

From April 2026: The gene content of the Adult onset neurological disorders panel includes all genes on Hereditary ataxia with onset in adulthood (R54), Adult onset dystonia, chorea or related movement disorder (R56) Adult onset neurodegenerative disorders (previously R58, now R458, R459, R460 & R461), Adult onset hereditary spastic paraplegia (R60)

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R460.1	Amyotrophic lateral sclerosis	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Adult onset neurological disorders (1669)	WGS

R460肌萎缩侧索硬化

检测标准

肌萎缩侧索硬化(ALS)，具有可能的单基因病因，伴或不伴额颞叶痴呆
和：

a. 临床、电生理或神经病理检查证实下运动神经元(LMN)变性，且
b. 临床检查显示上运动神经元(UMN)变性的证据，并且
c. 进行性病程，且
e. 无其他病因证据

通路中的位置

就诊时经神经科医师评估后

申请专科

• 临床遗传学
• 神经科
• 精神病学

专科服务组

• 神经科

相关检测

自2026年4月起：成人起病神经系统疾病panel的基因内容包含以下所有基因：成人起病遗传性共济失调(R54)、成人起病肌张力障碍、舞蹈症或相关运动障碍(R56)、成人起病神经退行性疾病(原R58，现为R458、R459、R460及R461)、成人起病遗传性痉挛性截瘫(R60)

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R460.1	肌萎缩侧索硬化	三人组或单人	外显子水平CNVs，小变异序列，短串联重复	基因组或基因座	成人起病神经系统疾病 (1669)	全基因组测序

R461 Cerebral amyloid angiopathy

Testing Criteria

Cerebral amyloid angiopathy (CAA) with a likely monogenic cause AND:

a. Age of onset < 50 years OR
b. Family history of haemorrhagic stroke (intracerebral haemorrhage or convexity subarachnoid haemorrhage) or dementia AND
c. Clinical presentation in keeping with CAA i.e. transient focal neurological episodes (“amyloid spells”), intracerebral haemorrhage, convexity subarachnoid haemorrhage, cognitive impairment, dementia AND
d. Radiological features consistent with CAA i.e. two or more strictly lobar haemorrhagic lesions on blood sensitive MRI, which can include intracerebral haemorrhage, cerebral microbleeds, cortical superficial siderosis or convexity subarachnoid haemorrhage OR
e. Other investigations supportive of amyloid-beta deposition within the central nervous system e.g. amyloid-PET imaging, CSF amyloid-beta measures, brain biopsy

Where in Pathway

At presentation following assessment by a Neurologist

Requesting Specialties

- Clinical Genetics
- Neurology
- Psychiatry

Specialist Service Group

- Neurology

Associated Tests

From April 2026: The gene content of the Adult onset neurological disorders panel includes all genes on Hereditary ataxia with onset in adulthood (R54), Adult onset dystonia, chorea or related movement disorder (R56) Adult onset neurodegenerative disorders (previously R58, now R458, R459, R460 & R461), Adult onset hereditary spastic paraplegia (R60)

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R461.1	Cerebral amyloid angiopathy	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Adult onset neurological disorders (1669)	WGS

R461脑淀粉样血管病

检测标准

伴可能单基因病因的脑淀粉样血管病(CAA)且：

a. 发病年龄< 50 岁 OR
b. 出血性卒中(脑出血或凸面蛛网膜下腔出血)或痴呆的家族史，且
c. 临床表现符合CAA，即短暂性局灶性神经发作(“淀粉样发作”)、脑出血、凸面蛛网膜下腔出血、认知障碍、痴呆，且
d. 影像学特征符合CAA，即在磁敏感MRI上出现两个或以上严格脑叶出血性病灶，可包括脑出血、脑微出血、皮质表面铁沉积或凸面蛛网膜下腔出血，或
e. 其他支持中枢神经系统内淀粉样蛋白-β沉积的检查，如淀粉样蛋白-PET成像、CSF淀粉样蛋白-β检测、脑活检

通路中的位置

就诊时经神经科医师评估后

申请专科

• 临床遗传学
• 神经科
• 精神病学

专科服务组

• 神经科

相关检测

自2026年4月起：成人起病神经系统疾病panel的基因内容包含以下所有基因：成人起病遗传性共济失调(R54)、成人起病肌张力障碍、舞蹈症或相关运动障碍(R56)、成人起病神经退行性疾病(原R58，现为R458、R459、R460及R461)、成人起病遗传性痉挛性截瘫(R60)

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R461.1	脑淀粉样血管病	三人组或单人	外显子水平CNVs，小变异，短串联重复序列	基因组或基因座	成人起病神经系统疾病 (1669)	全基因组测序

R60 Adult onset hereditary spastic paraplegia

Testing Criteria

Unexplained spastic paraplegia of likely monogenic aetiology with onset in adulthood

STR testing of spinocerebellar ataxia loci will be included as a component test where spinocerebellar ataxia is considered plausible clinically.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist or Clinical Geneticist

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

From April 2026: The gene content of the Adult onset neurological disorders panel includes all genes on Hereditary ataxia with onset in adulthood (R54), Adult onset dystonia, chorea or related movement disorder (R56) and Adult onset neurodegenerative disorders (previously R58, now R458, R459, R460 & R461) Adult onset hereditary spastic paraplegia (R60).

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R60.3	Adult onset hereditary spastic paraplegia WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Adult-onset neurological disorders (1669)	WGS

R60成人起病遗传性痉挛性截瘫

检测标准

不明原因的痉挛性截瘫，可能为单基因病因，成年起病

在临床上认为脊髓小脑共济失调合理的情况下，脊髓小脑共济失调位点的短串联重复序列检测将作为组成检测纳入。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在神经科医生或临床遗传学家评估后就诊时

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

自2026年4月起：成人起病神经系统疾病检测面板的基因内容包含遗传性成人起病共济失调(R54)、成人起病肌张力障碍、舞蹈症或相关运动障碍(R56)以及成人起病神经退行性疾病(原R58，现为R458、R459、R460和R461)、成人起病遗传性痉挛性截瘫(R60)的全部基因。

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R60.3	成人起病遗传性痉挛性截瘫全基因组测序(第2阶段)	三人组或单人 外显子水平	CNVs，小变异，短串联重复	基因检测板或基因座	成人起病神经系统疾病 (1669)	全基因组测序

R61 Childhood onset hereditary spastic paraplegia

Testing Criteria

Unexplained spastic paraplegia of likely monogenic aetiology with onset in childhood

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist or Clinical Geneticist

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R61.4	Hereditary spastic paraplegia - child onset WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants; STRs	Panel of genes or loci	Hereditary spastic paraplegia - Childhood onset (568)	WGS

R61儿童期起病遗传性痉挛性截瘫

检测标准

病因可能为单基因的儿童期起病不明原因痉挛性截瘫

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在神经科医生或临床遗传学家评估后就诊时

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R61.4	遗传性痉挛性截瘫 - 儿童发病 WGS（阶段 1）	三人组或单人 外显子水平	CNVs，小变异；短串联重复	基因检测板或基因座	遗传性痉挛性截瘫 - 儿童期起病（568）	全基因组测序

R62 Adult onset leukodystrophy

Testing Criteria

Individuals with unexplained leukodystrophy on neuroimaging with onset in adulthood

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following review of neuroimaging by Neuroradiologist

Referrals can be arranged via the Highly Specialised Service for Inherited White Matter Disorders, or directly by the specialties below. The HSS service supports centres in establishing diagnoses for patients, including via remote review MDTs. It also maintains a IWMD patient Registry and provides treatment and management advice to clinicians. Please contact uclh.iwmd@nhs.net or see https://www.uclh.nhs.uk/our-services/find-service/neurology-and-neurosurgery/inherited-white-matter-disorders for more details.

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R62.2	Adult onset leukodystrophy WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	White matter disorders - adult onset (579)	WGS

R62成人起病脑白质营养不良

检测标准

神经影像学显示不明原因脑白质营养不良的成年起病个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，经神经放射科医师复核神经影像后

可通过遗传性白质疾病高度专业化服务安排转诊，或直接由以下专科安排。HSS 服务支持各中心为患者确立诊断，包括通过远程病例讨论 MDT 进行。该服务还维护 IWMD 患者登记库，并向临床医生提供治疗和管理建议。请联系uclh.iwmd@nhs.net或参阅https://www.uclh.nhs.uk/our- services/find-service/neurology-and-neurosurgery/inherited-white-matter-disorders了解更多详情。

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R62.2	成人起病脑白质营养不良WGS(第二阶段)	三人组或单人	外显子水平CNVs，小变异	基因检测板或基因座	白质疾病 - 成人起病（579）	全基因组测序

R66 Paroxysmal central nervous system disorders

Testing Criteria

Paroxysmal central nervous system disorder that is likely to be monogenic in aetiology

Overlapping indications

- R56 Adult onset dystonia, chorea or related movement disorder or R57 Childhood onset dystonia, chorea or related movement disorder tests should be used in individuals with dystonia
- R89 Ultra-rare and atypical monogenic disorders or other relevant broader tests should be used in individuals with complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Consultant Neurologist or Paediatric Neurologist

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R66.1	Paroxysmal central nervous system disorders WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Paroxysmal central nervous system disorders (541)	WES or Medium Panel

R66阵发性中枢神经系统疾病

检测标准

病因可能为单基因的阵发性中枢神经系统疾病

重叠指征

- R56 成人起病肌张力障碍、舞蹈症或相关运动障碍或R57 儿童期起病肌张力障碍，舞蹈症或相关运动障碍检测应用于肌张力障碍个体
- R89 超罕见及非典型单基因疾病或其他相关更广泛检测应用于具有复杂或综合征性表现的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

经神经内科顾问医师或儿科神经内科顾问医师评估后就诊时

申请专科

- 临床遗传学
- 神经科

专科服务组

- 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R66.1	阵发性中枢神经系统疾病WES或中检测	单人	小变异，拷贝数变异	基因检测板或基因座	阵发性中枢神经系统疾病（541）	WES或Medium检测板

R73 Duchenne or Becker muscular dystrophy

Testing Criteria

1. Individuals with clinical features strongly suggestive of Duchenne or Becker muscular dystrophy AND elevated creatine kinase
2. Testing a female family member of an affected male known to have or likely to have had Duchenne or Becker muscular dystrophy, but without confirmed molecular diagnosis.

Overlapping indications

- R79 Congenital muscular dystrophy test should be considered following discussion with Neuromuscular specialist in atypical cases
- R381 Other rare neuromuscular disorders should be used where clinical features are atypical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Community Paediatrics
- Neurology
- Paediatrics

Specialist Service Group

- Neurology

Associated Tests

Please note all the tests below will be undertaken for R73 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R73.1	DMD Single gene sequencing	Singleton	Small variants	Single gene(s)	DMD (1321)	Single gene sequencing >=10 amplicons
R73.2	DMD MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	DMD (1321)	MLPA or equivalent

R73Duchenne或Becker肌营养不良

检测标准

1. 临床特征强烈提示Duchenne或Becker肌营养不良的个体
   以及肌酸激酶升高
2. 对已知患有或可能曾患有Duchenne的受累男性的女性家庭成员进行检测
   或贝克尔型肌营养不良症，但未经分子诊断确诊。

重叠指征

• R79 先天性肌营养不良检测应在与神经肌肉
非典型病例专家

• R381 其他罕见神经肌肉疾病应在临床特征不典型时使用，且检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理的个体。
更广泛的基因范围可能具有致病性

通路中的位置

申请专科

• 临床遗传学
• 社区儿科
• 神经科
• 儿科

专科服务组

• 神经科

相关检测

请注意，以下所有检测将针对R73临床指征请求进行，除非临床表现和/或初始结果提示所有检测均不必要代码

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R73.1	DMD单基因测序	单人	小变异	单基因	DMD(1321)	单基因测序 >=10扩增子
R73.2	DMD MLPA或等效	单人	外显子水平拷贝数变异	单基因	DMD(1321)	MLPA或等效

R74 Facioscapulohumeral muscular dystrophy

Testing Criteria

Clinical features strongly suggestive of facioscapulohumeral muscular dystrophy (FSHD) in whom a DUX4 contraction has not been excluded

Overlapping indications

- R82 Limb girdle muscular dystrophies, myofibrillar myopathies and distal myopathies and broader tests such as R89 Ultra-rare and atypical monogenic disorders should be considered where features are atypical
- R345 Facioscapulohumeral muscular dystrophy (FSHD) extended testing should be considered in cases negative for the test where clinical features are strongly suggestive of FSHD
- R381 Other rare neuromuscular disorders should be used where clinical features are atypical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R74.1	DUX4 Contraction testing	Singleton	STRs	Single interval	DUX4 STR	Other

R74面肩肱型肌营养不良

检测标准

临床特征强烈提示面肩肱型肌营养不良(FSHD)且尚未排除DUX4收缩的个体

重叠指征

• R82 肢带型肌营养不良、肌原纤维肌病和远端肌病及更广泛检测
如R89超罕见及非典型单基因疾病应在特征不典型时考虑

• R345 面肩肱型肌营养不良(FSHD)扩展检测应在检测阴性但临床特征强烈提示FSHD的病例中考虑

• R381 其他罕见神经肌肉疾病应在临床特征不典型且更广泛基因可能致病时使用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R74.1	DUX4收缩检测	单人	短串联重复序列	单一区间	DUX4 STR	其他

R345 Facioscapulohumeral muscular dystrophy - extended testing

Testing Criteria

Clinical features strongly suggestive of facioscapulohumeral muscular dystrophy (FSHD) in whom a DUX4 contraction has been excluded

Overlapping indications

- R74 Facioscapulohumeral muscular dystrophy test should be used where DUX4 contraction has not been excluded
- R82 Limb girdle muscular dystrophies, myofibrillar myopathies and distal myopathies and broader tests such as R381 Other rare neuromuscular disorders should be considered where features are atypical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following discussion with Neuromuscular consultant and/or testing laboratory

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R345.1	DUX4 Methylation testing	Singleton	Methylation	Single interval	DUX4	Methylation testing
R345.2	SMCHD1 Single gene sequencing	Singleton	Small variants	Single gene(s)	SMCHD1 (1324)	Single gene sequencing >=10 amplicons
R345.3	4q Extended testing	Singleton	Complex variants	Single interval	4q	Other

R345面肩肱型肌营养不良-扩展检测

检测标准

临床特征强烈提示面肩肱型肌营养不良(FSHD)且已排除DUX4收缩的个体

重叠指征

- R74 面肩肱型肌营养不良检测应在DUX4收缩尚未已被排除
- R82 肢带型肌营养不良、肌原纤维肌病和远端肌病及更广泛检测

如R381其他罕见神经肌肉疾病应在特征不典型时考虑检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理的个体。

通路中的位置

与神经肌肉顾问和/或检测实验室讨论后

申请专科

- 临床遗传学
- 神经科

专科服务组

- 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R345.1	DUX4甲基化检测	单人	甲基化	单一区间	DUX4	甲基化检测
R345.2	SMCHD1单基因测序	单人	小变异	单基因	SMCHD1 (1324)	单基因测序 >=10扩增子
R345.3	4q扩展检测单例		复合体变异	单一区间	4q	其他

R75 Oculopharyngeal muscular dystrophy

Testing Criteria

Clinical features strongly suggestive of oculopharyngeal muscular dystrophy

Overlapping indications

- R89 Ultra-rare and atypical monogenic disorders test should be considered where features are atypical
- R381 Other rare neuromuscular disorders should be used where clinical features are atypical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R75.1	PABPN1 STR testing	Singleton	STRs	Single gene(s)	PABPN1 STR	STR testing

R75眼咽型肌营养不良

检测标准

临床特征强烈提示眼咽型肌营养不良症

重叠指征

- R89 超罕见及非典型单基因疾病检测应在特征不典型时考虑
- 当临床特征不典型且存在其他罕见神经肌肉疾病时，应使用R381其他罕见神经肌肉疾病更广泛的基因范围可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 神经科

专科服务组

- 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R75.1	PABPN1 STR检测	单人	短串联重复序列	单基因	PABPN1 STR	STR检测

R76 Skeletal muscle channelopathy

Testing Criteria

Clinical features strongly suggestive of a skeletal muscle channelopathy including myotonia congenita or paramyotonia congenita

Overlapping indications

- R89 Ultra-rare and atypical monogenic disorders should be used where features are atypical
- R381 Other rare neuromuscular disorders should be used where clinical features are atypical and a broader range of genes are potentially causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation or following clinical assessment as part of the rare neuromuscular highly specialised service

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R76.1	Skeletal muscle channelopathy Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Skeletal muscle channelopathy (542)	Small panel

R76骨骼肌离子通道病

检测标准

临床特征强烈提示骨骼肌离子通道病，包括先天性肌强直或先天性副肌强直

重叠指征

• R89 超罕见和非典型单基因疾病应在特征不典型时使用

• 当临床特征不典型且存在其他罕见神经肌肉疾病时，应使用R381其他罕见神经肌肉疾病更广泛的基因范围可能具有致病性

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时或作为罕见神经肌肉高度专业化服务的一部分进行临床评估后

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R76.1	骨骼肌通道病 小panel	单人	小变异，拷贝数变异	基因检测板或基因座	骨骼肌通道病 (542)	小检测板

R78 Hereditary neuropathy or pain disorder

Testing Criteria

Clinical features that indicate a likely hereditary neuropathy or pain disorder in whom PMP22 copy number abnormalities are clinically unlikely or have already been excluded

Overlapping indications

- R77 Hereditary neuropathy - PMP22 copy number test should be used where PMP22 copy number abnormalities are possible
- R89 Ultra-rare and atypical monogenic disorders or R27 Paediatric disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Please note R78.5 (RFC1 STR) will not be included unless specifically requested.

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R78.4	Hereditary neuropathy or pain disorder number WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Hereditary neuropathy (846)	WGS
R78.5	*RFC1* STR	Singleton	STR	Single gene(s)	*RFC1 STR*	STR testing

R78遗传性神经病或疼痛障碍

检测标准

临床特征提示可能为遗传性神经病或疼痛障碍，且临床上 PMP22 拷贝数异常可能性不大或已被排除

重叠指征

• R77 遗传性神经病 - PMP22 拷贝数检测应在 PMP22 拷贝数
可能出现异常

• R89 超罕见和非典型单基因疾病或R27 儿科疾病检测应在以下个体中使用
患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

请注意，除非特别要求，R78.5(RFC1 STR)将不包含在内。

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R78.4	遗传性神经病或疼痛疾病编号 WGS(第二阶段)	三人组或单人 外显子水平	CNVs，小变异，短串联重复序列	基因组合或遗传性神经病基因座	(846) WGS	
R78.5	RFC1 短串联重复序列	单人	STR	单基因	RFC1 短串联重复序列	STR检测

R79 Congenital muscular dystrophy

Testing Criteria

Individuals with clinical features that indicate a likely congenital muscular dystrophy:

1. Muscle biopsy results indicative of congenital muscular dystrophy, OR
2. Muscle and/or brain MRI findings indicative of congenital muscular dystrophy

Overlapping indications

- R89 Ultra-rare and atypical monogenic disorders or R27 Paediatric disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations not typical of disorders covered by the panel

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist or following clinical assessment as part of the rare neuromuscular highly specialised service

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R79.1	Congenital muscular dystrophy WES or medium panel	Singleton	Small variants	Panel of genes or loci	Congenital muscular dystrophy (207)	WES or Medium Panel

R79先天性肌营养不良

检测标准

临床特征提示可能为先天性肌营养不良的个体：

1. 肌肉活检结果提示先天性肌营养不良，或
2. 肌肉和/或脑部 MRI 表现提示先天性肌营养不良

重叠指征

• R89 超罕见和非典型单基因疾病或R27 儿科疾病检测应在以下个体中使用
具有先天性畸形、畸形特征或其他复杂或综合征性表现，且非panel所涵盖疾病的典型表现

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经神经科医生评估后或作为罕见神经肌肉高度专业化服务的一部分进行临床评估后

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R79.1	先天性肌营养不良WES或中检测板	单人	小变异	基因检测板或基因座	先天性肌营养不良(207)	WES或Medium检测板

R80 Congenital myaesthenic syndrome

Testing Criteria

Clinical features that indicate a likely monogenic congenital myaesthenia

Overlapping indications

- R89 Ultra-rare and atypical monogenic disorders or R27 Paediatric disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations not typical of disorders covered by the panel

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist, typically in parallel to maternal anti-AChR antibody testing or following clinical assessment as part of the rare neuromuscular highly specialised service

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R80.1	Congenital myaesthenic syndrome WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Congenital myaesthenic syndrome (232)	WES or Medium Panel

R80先天性肌无力综合征

检测标准

提示可能为单基因先天性肌无力的临床特征

重叠指征

• R89 超罕见和非典型单基因疾病或R27 儿科疾病检测应在以下个体中使用
具有先天性畸形、畸形特征或其他复杂或综合征性表现，且非panel所涵盖疾病的典型表现

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经神经科医生评估后，通常与母体抗 AChR 抗体检测同时进行，或作为罕见神经肌肉高度专业化服务的一部分进行临床评估后

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R80.1	先天性肌无力综合征WES或中检	单人	小变异，拷贝数变异	基因检测板或基因座	先天性肌无力综合征（232）	WES或Medium检测板

R81 Congenital myopathy

Testing Criteria

Clinical or histopathological features that indicate a likely monogenic congenital myopathy

Overlapping indications

- R89 Ultra-rare and atypical monogenic disorders or R27 Paediatric disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations not typical of disorders covered by the panel

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist or following clinical assessment as part of the rare neuromuscular highly specialised service

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R81.1	Congenital myopathy WES or medium panel	Singleton	Small variants	Panel of genes or loci	Congenital myopathy (225)	WES or Medium Panel

R81先天性肌病

检测标准

临床或组织病理学特征提示可能为单基因先天性肌病

重叠指征

• R89 超罕见和非典型单基因疾病或R27 儿科疾病检测应在以下个体中使用
具有先天性畸形、畸形特征或其他复杂或综合征性表现，且非panel所涵盖疾病的典型表现

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经神经科医生评估后或作为罕见神经肌肉高度专业化服务的一部分进行临床评估后

申请专科

• 临床遗传学
• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R81.1	先天性肌病 WES 或中通量面板	单人	小变异	基因检测板或基因座	先天性肌病（225）	WES或Medium检测板

R82 Limb girdle muscular dystrophies, myofibrillar myopathies and distal myopathies

Testing Criteria

Clinical features that indicate a likely limb girdle muscular dystrophy or a genetic condition with overlapping phenotype such as distal myopathy or myofibrillar myopathy.

Overlapping indications

- R79 Congenital muscular dystrophy or R89 Ultra-rare and atypical monogenic disorders tests should be used where features are atypical

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist or referrals can be arranged via the Highly Specialised Service for Rare Neuromuscular Disorders in Newcastle. The HSS service supports centres in establishing diagnoses for patients by providing diagnostic advice including via remote review MDTs, in person clinical review of diagnosed and undiagnosed patients, and muscle biopsy immunoanalysis. Please contact nuth.hss.lgmd.referrals@nhs.net or visit https://jwmdrc.org/clinical-care

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R82.1	Limb girdle muscular dystrophies, myofibrillar myopathies and distal myopathies WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Limb girdle muscular dystrophies, myofibrillar myopathies and distal myopathies (185)	WES or Medium Panel

R82肢带型肌营养不良，肌原纤维肌病和远端肌病

检测标准

临床特征提示可能为肢带型肌营养不良或表型重叠的遗传性疾病，如远端肌病或肌原纤维肌病。

重叠指征

• R79 先天性肌营养不良或 R89 超罕见和非典型单基因疾病检测应使用检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家族管理的个体。

用于特征不典型的情况

通路中的位置

就诊时经神经科医生评估后，或可通过以下机构安排转诊：高度

专业化罕见神经肌肉疾病服务(纽卡斯尔)。HSS 服务通过提供诊断建议(包括通过远程审查 MDT、对已诊断和未诊断患者进行面对面临床审查以及肌肉活检免疫分析)支持各中心为患者确立诊断。请联系 nuth.hss.lgmd.referrals@nhs.net 或访问 https://jwmdrc.org/clinical-care

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R82.1	肢带型肌营养不良，肌原纤维性肌病和远端肌病 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	肢带型肌营养不良，肌原纤维性肌病和远端肌病（185）	WES或Medium检测板

R371 Malignant hyperthermia

Testing Criteria

Confident clinical diagnosis of malignant hyperthermia; anaesthetic history reviewed by MH investigation unit as appropriate. Reasons for referral:

1. Family history of malignant hyperthermia.
2. Adverse reaction to general anaesthesia where a trigger agent has been used, involving any combination of signs of increased metabolism (unexplained increase in carbon dioxide production, tachycardia, temperature increase, muscle rigidity, rhabdomyolysis, disseminated intravascular coagulation and/or death). Initial signs should be evident during anaesthesia or within 60 minutes of discontinuation of anaesthesia.
3. Family history of unexplained perioperative death suggestive of malignant hyperthermia.
4. Postoperative rhabdomyolysis after clinical exclusion of other myopathies.
5. Exertional rhabdomyolysis / recurrent rhabdomyolysis or persistently raised serum creatine kinase concentration of unknown cause (idiopathic hyperCKaemia) where no cause has been identified following neurological work-up.
6. Exertional heat stroke requiring hospital admission, where known predisposing factors have been excluded.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following discussion with national specialist service

Requesting Specialties

- Clinical Genetics
- Other

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R371.1	Malignant hyperthermia small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Malignant hyperthermia (1076)	Small panel

R371恶性高热

检测标准

恶性高热的明确临床诊断；麻醉史由 MH 调查单位酌情审查。转诊原因：

1. 恶性高热家族史。
2. 使用触发剂的全麻不良反应，涉及代谢增加体征的任何组合(二氧化碳产生不明原因增加、心动过速、体温升高、肌肉强直、横纹肌溶解、弥散性血管内凝血和/或死亡)。初始体征应在麻醉期间或停止麻醉后 60 分钟内出现。
3. 不明原因围手术期死亡的家族史，提示恶性高热。
4. 临床排除其他肌病后发生的术后横纹肌溶解症。
5. 劳力性横纹肌溶解/复发性横纹肌溶解或不明原因持续性血清肌酸激酶浓度升高(特发性高 CK 血症)，且神经系统检查后未确定病因。
6. 需要住院的劳力性热射病，且已排除已知易感因素。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

与国家专科服务讨论后

申请专科

• 临床遗传学

• 其他

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R371.1	恶性高热 小型检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	恶性高热 (1076)	小检测板

R83 Arthrogryposis

Testing Criteria

Clinical features that indicate arthrogryposis of monogenic aetiology

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following assessment by a Neurologist or Clinical Geneticist and following serum CK estimation

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R83.3	Arthrogryposis - broad panel WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Arthrogryposis (258)	WGS

R83关节挛缩

检测标准

提示单基因病因的关节挛缩症的临床特征

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经神经科医生或临床遗传学家评估后，并进行血清 CK 测定

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R83.3	关节挛缩 - 广泛面板 全基因组测序（第一阶段）	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	关节挛缩 (258)	全基因组测序

R381 Other rare neuromuscular disorders

Testing Criteria

Clinical features of rare neuromuscular disorder not covered by more specific indications

Overlapping indications

- Targeted tests for specific neuromuscular indications where relevant

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R381.2	Neuromuscular disorders WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants; STRs	Panel of genes or loci	Neuromuscular disorders (465)	WGS

R381其他罕见神经肌肉疾病

检测标准

未被更具体指征涵盖的罕见神经肌肉疾病的临床特征

重叠指征

• 针对相关特定神经肌肉适应症的靶向检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R381.2	神经肌肉疾病 全基因组测序（第一阶段）	三人组或单人 外显子水平	CNVs，小变异；短串联重复序列	基因检测板或基因座	神经肌肉疾病 (465)	全基因组测序

R84 Cerebellar anomalies

Testing Criteria

Likely monogenic cerebellar malformation, cerebellar or pontocerebellar hypoplasia or childhood-onset cerebellar atrophy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following MRI brain and assessment by a Neurologist or Clinical Geneticist

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R84.4	Hereditary ataxia and cerebellar anomalies - childhood onset WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Hereditary ataxia and cerebellar anomalies - childhood onset (488)	WGS

R84小脑异常

检测标准

可能为单基因小脑畸形、小脑或脑桥小脑发育不全或儿童期起病的小脑萎缩

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经脑部 MRI 和神经科医生或临床遗传学家评估后

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R84.4	遗传性共济失调和小脑异常 - 儿童期起病 WGS	三人组或单人（第 1 阶段）	外显子水平 CNVs，小变异，短串联重复	基因检测板或基因座	遗传性共济失调和小脑异常 - 儿童起病 (488)	全基因组测序

R85 Holoprosencephaly

Testing Criteria

Liveborn individuals with unexplained holoprosencephaly in whom a chromosomal cause is unlikely or has already been excluded by microarray or common aneuploidy testing .

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following chromosome microarray or common aneuploidy testing (which may have been prenatally through screening) unless a chromosomal cause is deemed less likely and a broader testing approach is appropriate.

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations
- R26 Likely common aneuploidy
- R28 Congenital malformation and dysmorphism syndromes – microarray

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R85.2	Holoprosencephaly WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Holoprosencephaly (78)	WGS

R85前脑无裂畸形

检测标准

患有不明显原因前脑无裂畸形的活产个体，且染色体原因可能性不大或已通过微阵列(基因芯片)或常见非整倍体检测排除。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时经染色体微阵列(基因芯片)或常见非整倍体检测(可能已通过产前筛查进行)后，除非认为染色体原因可能性较小且更广泛的检测方法合适。

重叠指征

- 对于存在先天性畸形、面容异常或其他复杂或综合征性表现的个体，应使用R27儿童期疾病或R89超罕见及非典型单基因疾病检测
- R26 可能为常见非整倍体
- R28 先天畸形与形态异常综合征--微阵列

申请专科

- 临床遗传学
- 神经科

专科服务组

- 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R85.2	前脑无裂畸形 WGS(第一阶段)	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	前脑无裂畸形 (78)	全基因组测序

R86 Hydrocephalus

Testing Criteria

Unexplained hydrocephalus with a likely monogenic cause, i.e. where secondary causes such as congenital infection and intraventricular haemorrhage are unlikely to be causative

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation after relevant acquired causes have been excluded where feasible

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R86.3	Hydrocephalus WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Hydrocephalus (179)	WGS

R86脑积水

检测标准

不明原因的脑积水，可能存在单基因病因，即先天性感染和脑室内出血等继发性原因不太可能是病因

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在排除相关获得性病因后(在可行情况下)就诊时

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R86.3	脑积水 WGS(第一阶段)	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	脑积水 (179)	全基因组测序

R87 Cerebral malformation

Testing Criteria

Cerebral malformation such as cortical malformation or porencephaly with features suggestive of a monogenic cause.

Overlapping indications

- R110 Segmental overgrowth disorders – Deep sequencing test should be used where megalencephaly is present to allow detection of mosaic variants

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R87.3	Cerebral malformations WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Cerebral malformations (491)	WGS

R87脑畸形

检测标准

脑畸形，如皮质畸形或脑穿通畸形，其特征提示
单基因病因。

重叠指征

• R110 节段性过度生长障碍--存在巨脑时应使用深度测序检测，以便检出嵌合变异

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R87.3	脑 畸形 WGS(第一阶段)	三人组或单人	外显子水平 CNVs，小 变异	基因检测板或 基因座	脑畸形 (491)	全基因组测序

R88 Severe microcephaly

Testing Criteria

Individuals with severe microcephaly* of likely monogenic aetiology.

*Severe microcephaly is defined as having an occipitofrontal circumference (OFC) beyond 3 standard deviations below the mean for age

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology
- Paediatrics

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R88.3	Severe microcephaly WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Severe microcephaly (162)	WGS

R88严重小头畸形

检测标准

患有严重小头畸形*且可能为单基因病因的个体。

*重度小头畸形定义为枕额围(OFC)低于年龄均值3个标准差以上

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 神经科

• 儿科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R88.3	严重小头畸形 全基因组测序（第一阶段）	三人组或单人	外显子水平CNVs，小变异	基因检测板或基因座	严重小头畸形 (162)	全基因组测序

R109 Childhood onset leukodystrophy

Testing Criteria

Unexplained leukodystrophy on neuroimaging with onset in childhood

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation following review of neuroimaging by Neuroradiologist

Referrals can be arranged via the Highly Specialised Service for Inherited White Matter Disorders, or directly by the specialties below. The HSS service supports centres in establishing diagnoses for patients, including via remote review MDTs. It also maintains a IWMD patient Registry and provides treatment and management advice to clinicians. Please contact gst-tr.gosh-iwmdr@nhs.net for clinics at Guys and St Thomas' and Great Ormond Street Hospitals in London, bwc.neurologysecretaries@nhs.net for clinics in Birmingham and Leedsth-tr.north-IWMD@nhs.net for clinics in Leeds.

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R109.3	White matter disorders - childhood onset WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	White matter disorders - childhood onset (496)	WGS

R109儿童期起病脑白质营养不良

检测标准

儿童期起病的神经影像学上不明原因的脑白质营养不良

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，经神经放射科医师复核神经影像后

可通过遗传性白质疾病高度专业化服务安排转诊，或由以下专科直接转诊。HSS服务支持各中心为患者确立诊断，包括通过远程MDT审查。它还维护IWMD患者登记库，并向临床医生提供治疗和管理建议。请联系gst-tr.gosh-iwmdr@nhs.net了解伦敦Guys and St Thomas'和Great Ormond Street医院的诊所，联系bwc.neurologysecretaries@nhs.net了解以下地区的诊所

伯明翰和Leedsth-tr.north-IWMD@nhs.net，用于利兹的诊所。

申请专科

• 临床遗传学

• 代谢医学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R109.3	白质疾病 - 儿童期发病 WGS(第一阶段)	三人组或单人	外显子水平 CNVs，小变异，短串联重复序列	基因检测板或基因座	白质疾病 - 儿童期发病 (496)	全基因组测序

R221 Familial tumours of the nervous system

Testing Criteria

1. Individual +/- family history fulfils clinical criteria for Neurofibromatosis Type 2 related schwannomatosis

a. Bilateral vestibular schwannomas, OR

b. Either 2 Major OR one Major and two Minor criteria

Major Criteria

i. Unilateral vestibular schwannoma

ii Parent or child with NF2 related schwannomatosis

iii Two or more meningioma

Minor Criteria (can count more than one of a type e.g. 2 schwannoma count as two minor criteria)

I Ependymoma

Ii Meningioma

Iii Schwannoma

Minor criteria (can count only once)

I Juvenile subcapsular or cortical cataract

Ii Retinal hamartoma (any age)

Iii Epiretinal membrane <40

2. Schwannoma:

a. Schwannoma diagnosed <30years

b. Unilateral vestibular schwannoma and non-intradermal schwannoma without other features of NF2-related schwannomatosis

c. . Two or more non-intradermal schwannomas (at least one biopsy-confirmed)

d. . One pathologically confirmed schwannoma AND, unilateral vestibular schwannoma, OR intracranial meningioma OR ≥1 FDR with Schwannomatosis

3. Multiple or young onset meningioma

a. . Meningioma diagnosed < 20 years

b. . Any clear Cell Meningioma

c. 2 meningioma <50 years or >2 any age

d. Meningioma AND one or more pathologically confirmed schwannoma

4. Other indications

a. Childhood retinal hamartoma

Note

Tumour-based testing checking for mosaicism will be required in certain circumstances. Please refer to relevant guidance available on the UK Cancer Genetics Group website.

NOTE: All tumours should be histologically confirmed

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation and/or following consultation with the NF2 highly specialised service

Requesting Specialties

- Clinical Genetics

R221家族性肿瘤的神经系统

检测标准

1. 个体+/-家族史符合2型神经纤维瘤病相关神经鞘瘤病的临床标准 a.双侧前庭神经鞘瘤，或 b.2项主要标准或1项主要标准和2项次要标准主要标准 i.单侧前庭神经鞘瘤

ii 患有NF2相关神经鞘瘤病的父母或子女 iii 两个或两个以上脑膜瘤

次要标准(同一类型可计数不止一项，例如2个神经鞘瘤计为两项次要标准) I 室管膜瘤

II 脑膜瘤

III 神经鞘瘤

次要标准(仅可计一次)

青少年囊膜下或皮质性白内障

Ii 视网膜错构瘤(任何年龄)

Iii 视网膜前膜<40

2. 神经鞘瘤：

a. 30岁前确诊的神经鞘瘤

b. 单侧前庭神经鞘瘤和非皮内神经鞘瘤，无NF2的其他特征-

相关神经鞘瘤病

c..两个或更多非皮内神经鞘瘤(至少一个经活检确认) d..一个经病理确认的神经鞘瘤且，单侧前庭神经鞘瘤，或颅内脑膜瘤或≥1名一级亲属患有神经鞘瘤病

3. **多发性或早发性脑膜瘤**

a. .脑膜瘤诊断年龄< 20 岁

b. 任何透明细胞脑膜瘤

c. 2例脑膜瘤<50岁或>2例任何年龄

d. 脑膜瘤 AND 一个或多个经病理证实的神经鞘瘤

4. **其他指征**

a. 儿童视网膜错构瘤

注

在某些情况下需要进行基于肿瘤的检测以检查嵌合现象。请参阅英国癌症遗传学组网站上提供的相关指南。

注：所有肿瘤均应经组织学确诊

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时和/或与NF2高度专业化服务咨询后

申请专科

• 临床遗传学

Specialist Service Group

- Neurology

Associated Tests

Please note all the tests below will be undertaken for R221 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R221.1	Familial tumours of the nervous system	Singleton	Small variants	Single genes	Familial tumours of the nervous system (1334)	Small panel
R221.2	Familial tumours of the nervous system	Singleton	Exon level CNVs	Single genes	Familial tumours of the nervous system (1334)	MLPA or equivalent

专科服务组

• 神经科

相关检测

请注意，以下所有检测将针对R221临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R221.1	家族性肿瘤 神经系统	单人	小变异	单基因	神经系统家族性肿瘤 系统 (1334)	小检测板
R221.2	家族性肿瘤 神经系统	单人	外显子水平 拷贝数变异	单基因	神经系统家族性肿瘤 系统 (1334)	MLPA或 等效

R222 Neurofibromatosis type 1

Testing Criteria

Clinical diagnosis of NF1, as defined below, AND molecular diagnosis is required for management of the proband or for reproductive planning

Diagnosis requires two of:

1. At least 6 café au lait macules (at least 0.5cm in a child and 1.5cm in an adult)
2. At least 2 subcutaneous or cutaneous neurofibromas
3. Plexiform neurofibroma
4. Optic glioma
5. At least 2 Lisch nodules
6. Bony dysplasia (sphenoid wing, long bone bowing, pseudarthrosis)
7. Family history of NF1
8. Axillary/inguinal freckling
9. Malignant Peripheral Nerve Sheath Tumour

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- R236 Pigmentary skin disorders test should be used where clinical features are atypical and a broader range of genes is potentially causative
- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Where in Pathway

At a point where clinical management or reproductive planning require a molecular diagnosis

Requesting Specialties

- Clinical Genetics
- Dermatology
- Neurology
- Paediatrics

Specialist Service Group

- Neurology

Associated Tests

Please note all the tests below will be undertaken for R222 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R222.1	NF1; SPRED1 Single gene sequencing	Singleton	Small variants	Single gene(s)	NF1; SPRED1 (1370)	Small panel
R222.2	NF1; SPRED1 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	NF1; SPRED1 (1370)	MLPA or equivalent

R222神经纤维瘤病1型

检测标准

NF1的临床诊断，定义如下，且分子诊断对于先证者的管理或生育计划是必需的。诊断需满足以下两项：

1. 至少6个牛奶咖啡斑(儿童至少0.5cm，成人至少1.5cm)
2. 至少2个皮下或皮肤神经纤维瘤
3. 丛状神经纤维瘤
4. 视神经胶质瘤
5. 至少2个Lisch结节
6. 骨发育不良(蝶骨翼、长骨弯曲、假关节)
7. NF1家族史
8. 腋窝/腹股沟雀斑
9. 恶性外周神经鞘瘤

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

- 当临床特征不典型且需要更广泛的鉴别诊断时，应使用R236色素性皮肤疾病检测基因范围可能具有致病性
- R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于存在先天性畸形、面容异常或其他复杂或综合征性表现的个体

通路中的位置

在临床管理或生殖计划需要分子诊断的情况下

申请专科

- 临床遗传学
- 皮肤病学
- 神经科
- 儿科

专科服务组

- 神经科

相关检测

请注意，以下所有检测将针对R222临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R222.1	NF1；SPRED1 单基因测序	单人	小变异	单基因	NF1；SPRED1 (1370)	小检测板
R222.2	NF1；SPRED1 MLPA或等效方法	单人	外显子水平拷贝数变异	单基因	NF1；SPRED1 (1370)	MLPA或等效

R376 Segmental or atypical neurofibromatosis type 1 testing

Testing Criteria

Clinical features suggestive of segmental or atypical neurofibromatosis type 1 or individuals with classical neurofibromatosis who have tested negative on gDNA analysis requiring cDNA analysis following discussion with highly specialised service

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following consultation with highly specialised service

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Please note all the tests below will be undertaken for R376 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R376.1	NF1 Single gene sequencing – mosaic	Singleton	Small variants	Single gene(s)	NF1 (1387)	Single gene sequencing >=10 amplicons
R376.2	NF1 MLPA or equivalent – mosaic	Singleton	Exon level CNVs	Single gene(s)	NF1 (1387)	MLPA or equivalent

R376节段性或非典型神经纤维瘤病1型检测

检测标准

临床特征提示节段性或非典型神经纤维瘤病1型，或经典型神经纤维瘤病患者在gDNA分析检测阴性后，经与高度专业化服务团队讨论需要进行cDNA分析

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在与高度专业化服务部门协商后

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

请注意，以下所有检测将针对R376临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R376.1	NF1单基因测序 – 嵌合	单人	小变异	单基因	NF1(1387)	单基因测序 >=10扩增子
R376.2	NF1 MLPA或等效 – 嵌合	单人	外显子水平拷贝数变异	单基因	NF1(1387)	MLPA或等效

R228 Tuberous sclerosis

Testing Criteria

Clinical features suggestive of tuberous sclerosis requiring molecular testing

Testing should typically be targeted at those with one or more major features or two or more minor features:

1. Major features:
   a. Hypomelanotic macules (at least 3 of at least 5 mm in diameter)
   b. Angiofibromas (at least three) or fibrous cephalic plaque
   c. Ungual fibromas (at least two)
   d. Shagreen patch
   e. Multiple retinal hamartomas
   f. Cortical dysplasias characteristic of tuberous sclerosis such as tubers and cerebral white matter radial migration lines
   g. Subependymal nodules
   h. Subependymal giant cell astrocytoma
   i. Cardiac rhabdomyomas
   j. Lymphangioleiomyomatosis (LAM)
   k. Angiomyolipomas (at least two)
2. Minor features:
   a. Confetti skin lesions
   b. Dental enamel pits (>3)
   c. Intraoral fibromas (at least two)
   d. Retinal achromic patch
   e. Multiple renal cysts
   f. Non- renal hamartomas

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Fetal Medicine
- Nephrology
- Neurology
- Respiratory Medicine

Specialist Service Group

- Neurology

Associated Tests

Please note R228.1 and R228.2 will be undertaken for all R228 Clinical Indication requests and R228.3 will only be undertaken where a pathogenic variant has not been found on R228.1 and R228.2

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R228.1	TSC1; TSC2	Singleton	Small variants	Small panel	TSC1; TSC2 (1400)	Small panel

R228结节性硬化症

检测标准

提示结节性硬化症、需进行分子检测的临床特征

检测通常应针对具有一项或多项主要特征或两项或多项次要特征的患者：

1. 主要特征：
   a. 色素减退斑(至少3个，直径至少5 mm)
   b.血管纤维瘤(至少三个)或纤维性头斑 c.甲周纤维瘤(至少两个)
   d. 鲨鱼皮斑
   e. 多发性视网膜错构瘤
   f. 结节性硬化症特征性的皮质发育不良，如结节和脑白质放射状迁移线
   g. 室管膜下结节
   h. 室管膜下巨细胞星形细胞瘤
   i. 心脏横纹肌瘤
   j. 淋巴管肌瘤病(LAM)
   k. 血管平滑肌脂肪瘤(至少两个)
2. 次要特征：
   a. 五彩纸屑样皮肤病变
   b. 牙釉质凹坑(>3)
   c. 口腔内纤维瘤(至少两个)
   d. 视网膜色素脱失斑
   e. 多发性肾囊肿
   f. 非肾错构瘤

重叠指征

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 临床遗传学
• 胎儿医学
• 肾脏科
• 神经科
• 呼吸医学

专科服务组

• 神经科

相关检测

请注意，R228.1和R228.2将针对所有R228临床指征请求进行，R228.3仅在R228.1和R228.2未发现致病变异时进行

	名称	最佳家族结构	范围	目标类型	目标名称	方法
R228.1	TSC1;TSC2	单人	小检测板变异	小检测板	TSC1；TSC2 (1400)	小检测板

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R228.2	TSC1; TSC2 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	TSC1; TSC2 (1400)	MLPA or equivalent
R228.3	TSC1; TSC2 – Small panel deep sequencing	Singleton	Small variants	Small panel	TSC1; TSC2 (1400)	Small panel – deep sequencing

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R228.2	TSC1；TSC2 MLPA或等效	单人	外显子水平拷贝数变异	单基因	TSC1；TSC2 (1400)	MLPA或等效方法
R228.3	TSC1；TSC2 – 小检测板深度测序	单人	小检测板变异	小检测板	TSC1；TSC2 (1400)	小检测板 – 深度测序

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R294 Ataxia telangiectasia – DNA repair testing

Testing Criteria

1. Clinical features strongly suggestive of ataxia telangiectasia including elevated serum AFP levels, AND one or more of the following:
   a. Progressive gait and truncal ataxia with onset between one and four years of age, OR
   b. Ocular motor apraxia, OR
   c. Ocular telangiectasia, OR
   d. Chorea and dysarthria, OR
   e. Immunodeficiency with frequent infections, OR
   f. Malignancy (e.g. leukaemia and lymphoma, breast cancer, ovarian cancer gastric cancer, leiomyoma, sarcoma or melanoma), OR
2. Molecular findings suggestive of Fanconi anaemia or Bloom syndrome from genome, exome or other genomic analysis

Overlapping indications

- R27 Paediatric disorders, R89 Ultra-rare and atypical monogenic disorders or other broad genomic tests should typically be used except where the above criteria are fulfilled
- Prenatal diagnosis or cascade testing by chromosome breakage testing will be requested via R240 Diagnostic testing for known familial variant(s)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Oncology
- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R294.1	Genomewide DNA repair defect testing	Singleton	DNA repair	Genomewide	Genomewide	DNA repair defect testing

R294共济失调毛细血管扩张症-DNA修复检测

检测标准

1. 临床特征强烈提示共济失调毛细血管扩张症，包括血清AFP水平升高，且以下一项或多项：
   a. 进行性步态和躯干共济失调，发病年龄在1至4岁之间，或
   b. 眼动失用症，OR
   c. 眼部毛细血管扩张，OR
   d. 舞蹈症和构音障碍，OR
   e. 伴频繁感染的免疫缺陷，或
   f. 恶性肿瘤(如白血病和淋巴瘤、乳腺癌、卵巢癌、胃癌、平滑肌瘤、肉瘤或黑色素瘤)，或
2. 基因组、外显子组或其他基因组分析提示范可尼贫血或Bloom综合征的分子发现

重叠指征

• R27儿科疾病、R89超罕见和非典型单基因疾病或其他广泛基因组检测通常应使用，除非满足上述标准

• 产前诊断或通过染色体断裂检测进行的级联检测将通过R240申请针对已知家族变异的诊断检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 肿瘤学

• 临床遗传学

• 血液学

• 免疫学

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R294.1	全基因组范围DNA修复缺陷检测	单人	DNA修复	全基因组范围	全基因组范围	DNA修复缺陷检测

R295 Ataxia telangiectasia – variant testing

Testing Criteria

Confirmed diagnosis of ataxia telangiectasia requiring variant testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

After DNA repair testing

Requesting Specialties

- Oncology
- Clinical Genetics
- Haematology
- Immunology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R295.1	ATM Single gene sequencing	Singleton	Small variants	Single gene(s)	ATM (1213)	Single gene sequencing >=10 amplicons

R295共济失调毛细血管扩张症-变异检测

检测标准

确诊共济失调毛细血管扩张症需进行变异检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

DNA 修复检测后

申请专科

• 肿瘤学
• 临床遗传学
• 血液学
• 免疫学

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R295.1	ATM单基因测序	单人	小变异	单基因	ATM(1213)	单基因测序 >=10扩增子

R336 Cerebral vascular malformations

Testing Criteria

1. Multiple cerebral vascular malformations, OR
2. Cerebral vascular malformation AND family history of cerebral vascular malformation

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following neuroimaging

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R336.1	Cerebral vascular malformations WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Cerebral vascular malformations (147)	WES or Medium Panel

R336脑血管畸形

检测标准

1. 多发性脑血管畸形，OR
2. 脑血管畸形且具有脑血管畸形家族史

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

以下神经影像学检查

申请专科

• 临床遗传学
• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R336.1	脑血管畸形 WES或中等 panel	单人	小变异，拷贝数变异	基因检测板或基因座	脑血管畸形 (147)	WES或Medium检测板

R337 CADASIL

Testing Criteria

A confident clinical diagnosis of CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) including:

Cerebral ischaemic event below age of 50 or >50 if with a family history of dementia/migraine, AND one or more of:

1. Cognitive impairment with recurrent ischaemic attacks, OR
2. Subcortical lacunar lesions on MRI scan in white matter

Overlapping indications

- R461 Cerebral amyloid angiopathy should be used where a broader differential diagnosis is under consideration

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R337.1	NOTCH3 Single gene sequencing	Singleton	Small variants	Single gene(s)	NOTCH3 (1311)	Single gene sequencing >=10 amplicons

R337 CADASIL

检测标准

CADASIL(伴皮质下梗死和白质脑病的常染色体显性遗传性脑动脉病)的明确临床诊断，包括：

50岁以下发生脑缺血事件，或50岁以上但具有痴呆/偏头痛家族史，且满足以下一项或多项：

1. 认知障碍伴反复缺血性发作，或
2. MRI 扫描显示白质皮质下腔隙性病变

重叠指征

• 当需要更广泛的鉴别诊断时，应使用R461脑淀粉样血管病检测
考虑

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 神经科

专科服务组

• 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R337.1	NOTCH3单基因测序	单人	小变异	单基因	NOTCH3 (1311)	单基因测序 >=10扩增子

R410 Myotonic dystrophy type 2 (DM2)

Testing Criteria

1. Adult with muscle weakness, usually proximal, and one of the following:
   a. Clinical Myotonia: of grip or on percussion
   b. EMG evidence of myotonic discharges
   c. Cataracts (fine dust like opacities on the outer layers of the lens that are highly coloured and iridescent, producing a “Christmas Tree” appearance)
   d. Three or more supportive features (from list below)
   e. Family History suggestive of autosomal dominant inheritance

2. **AND** DM1 excluded first if the clinical presentation/Family history could easily fit DM1
3. **OR** Family history of variant positive DM2

Additional supportive features:

- Elevated serum CK
- Insulin-insensitive type 2 diabetes
- Testicular failure
- Cardiac conduction defects
- Low serum IgG or IgM
- Muscle biopsy showing atrophic fibres and proliferation of fibres with central nuclei
- Excessive daytime sleepiness
- Mildly elevated liver function tests (LFT)
- Muscle pain

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- R72 Myotonic dystrophy type 1 should be used prior to this indication unless there is clinical suspicion of myotonic dystrophy type 2
- R381 Other rare neuromuscular disorders should be used where clinical features are atypical and a broader range of genes are potentially causative

Where in Pathway

At presentation, following a normal test for Myotonic dystrophy type 1, unless there is clinical suspicion of myotonic dystrophy type 2

Requesting Specialties

- Clinical Genetics
- Neurology

Specialist Service Group

- Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R410.1	CNBP (ZNF9) STR testing	Singleton	Short tandem repeats	Single gene(s)	CNBP (ZNF9)	STR testing

R410强直性营养不良2型2(DM2)

检测标准

1. 成人出现肌无力，通常为近端，并具备以下之一：
   a.临床肌强直：握拳或叩击时 b.肌电图显示肌强直放电
   c. 白内障(晶状体外层细粉尘样混浊，高度着色并呈虹彩，呈现“圣诞树”外观)
   d. 三个或以上支持性特征(来自以下列表)
   e. 家族史提示常染色体显性遗传

2. **且**如果临床表现/家族史容易符合DM1，首先排除DM1
3. **或**变异阳性DM2家族史

附加支持性特征：

- 血清CK升高
- 胰岛素不敏感型2型糖尿病
- 睾丸功能衰竭
- 心脏传导缺陷
- 血清IgG或IgM降低
- 肌肉活检显示萎缩纤维及中央核纤维增生
- 日间过度嗜睡
- 肝功能检查(LFT)轻度升高
- 肌肉疼痛

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

- 在此指征之前应使用R72强直性肌营养不良1型，除非临床怀疑2型强直性肌营养不良
- 当临床特征不典型且存在其他罕见神经肌肉疾病时，应使用R381其他罕见神经肌肉疾病更广泛的基因范围可能具有致病性

通路中的位置

就诊时，强直性肌营养不良1型检测正常后，除非临床怀疑强直性肌营养不良2型

申请专科

- 临床遗传学
- 神经科

专科服务组

- 神经科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R410.1	CNBP (ZNF9) STR检测	单人	短串联重复	单基因	CNBP (ZNF9)	STR检测

R419 Acute Rhabdomyolysis

Testing Criteria

Any patient (including children) presenting with an acute rise in skeletal muscle CK>20,000 iu/l regardless of the trigger, unless this occurs following a single episode of unaccustomed exercise not requiring hospital admission e.g. following weight lifting, a personal trainer session, spin class, marathon etc. However, a second similar episode should trigger testing.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- R371 Malignant hyperthermia

Where in Pathway

At presentation or following clinical assessment as part of the McArdle Disease and related disorders highly specialised service

Requesting Specialties

- Neurology
- Intensive Care
- Clinical genetics
  Metabolic medicine
- Nephrology

Specialist Service Group

Neurology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R419.1	Acute Rhabdomyolysis Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Panel is being created in PanelApp	Medium panel

R419急性横纹肌溶解

检测标准

任何患者(包括儿童)表现为骨骼肌CK急性升高>20,000 iu/l，无论诱因如何，除非发生在单次不习惯运动后且无需住院，例如举重、私人教练课程、动感单车课、马拉松等。然而，第二次类似发作应触发检测。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

- R371 恶性高热

通路中的位置

就诊时或作为McArdle病及相关疾病高度专业化服务的一部分进行临床评估后

申请专科

- 神经科
- 重症监护
- 临床遗传学
  代谢医学
- 肾脏科

专科服务组

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R419.1	急性横纹肌溶解 中等 Panel	单人	小变异，拷贝数变异	基因检测板或基因座	检测板正在创建中 PanelApp	中检测板

Part XVIII. Renal

R193 Cystic renal disease

Testing Criteria

1. Patients with non-syndromic cystic renal disease (excluding acquired cystic disease due to chronic or end stage kidney disease) which is EITHER
2. Clinically not characteristic of ADPKD and underlying diagnosis is required for management purposes, OR
3. Clinically symptomatic disease presenting before the age of 18, OR
4. Clinical diagnosis of ADPKD where a genetic diagnosis is required to influence management

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, or when clinical management decision depending on molecular diagnosis is required

Requesting Specialties

- Clinical Genetics
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R193.4	Cystic renal disease WGS (phase 1)	Trio or Singleton	Exon level CNVs, Small variants	Panel of genes or loci	Cystic renal disease (487)	WGS

第XVIII部分肾脏

R193囊性肾病

检测标准

1. 非综合征性囊性肾病患者(排除由慢性或终末期肾病导致的获得性囊性疾病)，其符合以下任一条件
2. 临床不符合ADPKD特征且出于管理目的需要明确基础诊断，或
3. 18岁前出现临床症状性疾病，或
4. ADPKD临床诊断且需要遗传诊断以影响管理

重叠指征

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

就诊时，或需要根据分子诊断做出临床管理决策时

申请专科

• 临床遗传学

• 肾脏科

专科服务组

• 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R193.4	囊性肾疾病 WGS（第一阶段）	三人组或单人	外显子水平 CNVs，小变异	基因检测板或基因座	囊性肾病 (487)	全基因组测序

R194 Haematuria

Testing Criteria

Proband with haematuria and ONE of:

1. A first degree relative with haematuria or unexplained chronic renal failure, OR
2. Histological evidence following electron microscopy on renal biopsy of EITHER Alport syndrome (thickening and splitting of glomerular basement membrane +/- electron lucent areas) OR thin basement membrane disease (TBMD), OR
3. Clinical features of Alport syndrome (high tone sensorineural hearing loss or characteristic ophthalmic signs such as perimacular flecks or anterior lenticonus)

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations
- R196 CFHR5 nephropathy test should be used as a first line test in patients of Cypriot ancestry with haematuria

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Audiology
- Clinical Genetics
- Nephrology
- Ophthalmology
- Paediatrics

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R194.1	Haematuria Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Haematuria (99)	Small panel

R194血尿

检测标准

先证者有血尿并具备以下之一：

1. 一级亲属有血尿或不明原因的慢性肾功能衰竭，或
2. 肾活检电子显微镜下的组织学证据显示以下任一：Alport综合征(肾小球基底膜增厚和劈裂+/-电子透亮区)或薄基底膜病(TBMD)，或
3. Alport综合征的临床特征(高调感音神经性听力损失或特征性眼部体征如黄斑周围斑点或前圆锥晶状体)

重叠指征

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
患有先天性畸形、畸形特征或其他复杂或综合征性表现的患者 • 对于塞浦路斯血统患者，应使用R196 CFHR5肾病检测作为一线检测
血尿

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 听力学
• 临床遗传学
• 肾脏科
• 眼科
• 儿科

专科服务组

• 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R194.1	血尿 小检测板检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	血尿 (99)	小检测板

R195 Proteinuric renal disease

Testing Criteria

1. Steroid-resistant nephrotic syndrome presenting at any age, OR
2. Proteinuria with a histological picture of focal segmental glomerulosclerosis (FSGS) or diffuse mesangial sclerosis (DMS) on biopsy, with no identifiable cause, where a transplant or immunosuppression is planned

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, or at a time when management requires a molecular diagnosis

Requesting Specialties

- Clinical Genetics
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R195.3	Proteinuric renal disease	Trio or Singleton	Small variants, CNVs	Panel of genes or loci	Proteinuric renal disease (106)	WGS

R195蛋白尿性肾脏疾病

检测标准

1. 任何年龄发病的类固醇耐药性肾病综合征，或
2. 蛋白尿伴活检组织学表现为局灶节段性肾小球硬化(FSGS)或弥漫性系膜硬化(DMS)，无可识别病因，且计划进行移植或免疫抑制治疗

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，或在临床管理需要分子诊断时

申请专科

- 临床遗传学
- 肾脏科

专科服务组

- 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R195.3	蛋白尿性肾病	三人组或单人	小变异，拷贝数变异	基因检测板或基因座	蛋白尿性肾病 (106)	全基因组测序

R196 CFHR5 nephropathy

Testing Criteria

C3 glomerulopathy or unexplained haematuria or renal failure in a patient of Cypriot ancestry

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R196.1	CFHR5 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	CFHR5	MLPA or equivalent

R196CFHR5肾病

检测标准

塞浦路斯血统患者的C3肾小球病或不明原因血尿或肾衰竭

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 肾脏科

专科服务组

• 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R196.1	CFHR5 MLPA或等效	单人	外显子水平拷贝数变异	单基因	CFHR5	MLPA或等效

R197 Membranoproliferative glomerulonephritis including C3 glomerulopathy

Testing Criteria

Idiopathic membranoproliferative glomerulonephritis (MPGN) or C3 glomerulopathy with onset before the age of 18, together with one of:

1. Family history of MPGN or unexplained end-stage renal disease, OR
2. Renal transplant is being considered, OR
3. Patient is being considered for complement inhibitory therapies

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, or at a time when management requires a molecular diagnosis or following assessment as part of the highly specialised atypical haemolytic uraemic syndrome service

Requesting Specialties

- Clinical Genetics
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Please note all the tests below will be undertaken for R197 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R197.1	Membranoproliferative glomerulonephritis Small panel	Singleton	Small variants	Panel of genes or loci	Membranoproliferative glomerulonephritis (83)	Small panel
R197.2	Membranoproliferative glomerulonephritis MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	Membranoproliferative glomerulonephritis (83)	MLPA or equivalent

R197膜增生性肾小球肾炎包括C3肾小球病

检测标准

18岁前发病的特发性膜增生性肾小球肾炎(MPGN)或C3肾小球病，并伴有以下之一：

1. MPGN 家族史或不明原因的终末期肾病，或
2. 正在考虑肾移植，或
3. 正在考虑对患者使用补体抑制疗法

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，或在管理需要分子诊断时，或作为高度专业化非典型溶血性尿毒症综合征服务的一部分进行评估后

申请专科

• 临床遗传学

• 肾脏科

专科服务组

• 肾脏

相关检测

请注意，对于R197临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明所有检测均不必要

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R197.1	膜增生性肾小球肾炎小panel	单人	小变异	基因检测板或基因座	膜增生性肾小球肾炎 (83)	小检测板
R197.2	膜增生性肾小球肾炎MLPA 或等效方法	单人	外显子水平拷贝数变异	单基因	膜增生性肾小球肾炎 (83)	MLPA或等效

R198 Renal tubulopathies

Testing Criteria

Patients with a primary renal tubulopathy presenting as one of the following conditions:

1. Hypokalaemic alkalosis with normal or low blood pressure (e.g. Bartter/Gitelman syndromes), OR
2. Hypokalaemic alkalosis with elevated blood pressure (e.g. Liddle syndrome), OR
3. Hyperkalaemic acidosis with low/normal BP (PHA type 1), OR
4. Hyperkalaemic acidosis with elevated BP (PHA type 2), OR
5. Hypokalaemic acidosis (pRTA and renal Fanconi syndromes), OR
6. Hypomagnesaemia, OR
7. Nephrogenic diabetes insipidus, OR
8. Other rare types of renal tubulopathy seen in an expert center

NOTE: Patients with electrolyte imbalance secondary to non-renal processes should not be tested under this indication

Overlapping indications

- R183 Glucocorticoid-remediable aldosteronism (GRA)
- R344 Primary hyperaldosteronism – KCNJ5
- R256 Nephrocalcinosis or nephrolithiasis

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R198.1	Renal tubulopathies WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Renal tubulopathies (292)	WES or Medium Panel

R198肾小管病

检测标准

表现为以下情况之一的原发性肾小管病患者：

1. 伴血压正常或偏低的低钾性碱中毒(如 Bartter/Gitelman 综合征)，或
2. 低钾性碱中毒伴血压升高(例如 Liddle 综合征)，或
3. 高钾性酸中毒伴低/正常血压(PHA 1型)，或
4. 高钾性酸中毒伴血压升高(PHA 2型)，或
5. 低钾性酸中毒(pRTA 及肾 Fanconi 综合征)，或
6. 低镁血症，OR
7. 肾性尿崩症，OR
8. 专家中心见到的其他罕见类型肾小管病

注：继发于非肾脏过程的电解质紊乱患者不应按此指征进行检测

重叠指征

• R183 糖皮质激素可治性醛固酮增多症(GRA)

• R344 原发性醛固酮增多症 - KCNJ5

• R256 肾钙质沉着症或肾结石

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 肾脏科

专科服务组

• 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R198.1	肾小管病 WES或中等检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	肾小管病（292）	WES或Medium检测板

R199 Congenital anomalies of the kidney and urinary tract – familial

Testing Criteria

Clinically significant non-syndromic congenital anomalies of the kidney and urinary tract (CAKUT), with a first degree relative with CAKUT or unexplained end-stage renal disease

Families in which there are only minor forms of CAKUT are unlikely to benefit from genetic testing (e.g. isolated vesico-ureteric reflux, duplex kidney, posterior urethral valves)

Overlapping conditions:

- R141 Monogenic diabetes test should be used where there is a personal or family history of diabetes or renal cysts
- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Nephrology
- Paediatrics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R199.1	Genomewide Microarray	Singleton	Genomewide CNVs	Genomewide	Genomewide	Microarray

R199先天畸形肾脏和泌尿道-家族性

检测标准

具有临床意义的非综合征性先天畸形 of the kidney and urinary tract(CAKUT)，且有一级亲属患有 CAKUT 或不明原因终末期肾病

仅有轻微型 CAKUT 的家族不太可能从基因检测中获益(如孤立性膀胱输尿管反流、重复肾、后尿道瓣膜)重叠疾病：

• R141 单基因糖尿病检测应在有糖尿病个人史或家族史时使用，或
肾囊肿

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
患有先天性畸形、畸形特征或其他复杂或综合征表现的个体。检测转诊将由基因组实验室进行分诊；检测应针对那些基因或基因组诊断将指导先证者或家庭管理的人。

通路中的位置

申请专科

• 临床遗传学

• 肾脏科

• 儿科

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R199.1	全基因组范围 微阵列（基因芯片）	单人	全基因组范围 拷贝数变异	全基因组范围	全基因组范围	微阵列（基因芯片）

R201 Atypical haemolytic uraemic syndrome

Testing Criteria

Acute renal failure AND thrombocytopenia AND microangiopathic haemolytic anaemia (Coombs test negative), in a patient being considered for complement inhibitory therapies

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation or following assessment as part of the highly specialized atypical haemolytic uraemic syndrome service

Requesting Specialties

- Clinical Genetics
- Haematology
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R201.1	Atypical haemolytic uraemic syndrome Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Atypical haemolytic uraemic syndrome (139)	Small panel

R201非典型溶血性尿毒症综合征

检测标准

急性肾衰竭 AND 血小板减少 AND 微血管病性溶血性贫血(Coombs 试验阴性)，且患者正被考虑接受补体抑制治疗

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时或作为高度专业化非典型溶血性尿毒症评估的一部分
综合征服务

申请专科

- 临床遗传学
- 血液学
- 肾脏科

专科服务组

- 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R201.1	非典型溶血性尿毒症综合征小panel	单人	小变异，拷贝数变异	基因检测板或基因座	非典型溶血性尿毒症综合征（139）	小检测板

R202 Tubulointerstitial kidney disease

Testing Criteria

1. Renal impairment caused by tubulointerstitial fibrosis with no glomerular lesion, with no identifiable cause, often associated with medullary cysts, hyperuricaemia or gout, AND
2. A first degree relative with TIKD or unexplained end-stage renal disease. Exceptions may be made for patients where the clinical presentation is highly suggestive of a monogenic aetiology, but family history is unknown eg. the patient was adopted

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R202.1	Tubulointerstitial kidney disease Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Tubulointerstitial kidney disease (548)	Small panel

R202肾小管间质性肾脏疾病

检测标准

1. 由无肾小球病变的肾小管间质纤维化所致肾功能损害，无可识别病因，常与髓质囊肿、高尿酸血症或痛风相关，AND

2. 一级亲属患有 TIKD 或不明原因终末期肾病。对于临床表现高度提示单基因病因但家族史未知的患者(如患者为被收养者)，可作例外处理

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 肾脏科

专科服务组

• 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R202.1	肾小管间质性肾病 小\panel	单人	小变异，拷贝数变异	基因检测板或基因座	肾小管间质性肾病 (548)	小检测板

R204 Hereditary systemic amyloidosis

Testing Criteria

Clinical features suggestive of hereditary amyloidosis which may include restrictive cardiomyopathy, autonomic and peripheral neuropathy, renal impairment or GI symptoms.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics
- Nephrology
- Neurology
- Haematology
- Gastroenterology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R204.1	Hereditary systemic amyloidosis Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Amyloidosis (502)	Small panel

R204遗传性系统性淀粉样变性

检测标准

提示遗传性淀粉样变性的临床特征，可能包括限制性心肌病、自主神经及周围神经病、肾功能损害或胃肠道症状。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 心脏病学
- 临床遗传学
- 肾脏科
- 神经科
- 血液学
- 胃肠病学

专科服务组

- 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R204.1	遗传性系统性淀粉样变性 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	淀粉样变性（502）	小检测板

R256 Nephrocalcinosis or nephrolithiasis

Testing Criteria

Nephrocalcinosis or nephrolithiasis where acquired causes have been excluded

Overlapping indications

- Where a primary endocrine disturbance of calcium homeostasis is identified, the appropriate specific test should be used
- In individuals with an identifiable primary renal disorder, the specific test for that disorder should be used where genetic testing is appropriate
- Individuals with nephrocalcinosis likely to be caused by Bartter syndrome can be tested using this indication; individuals with a different presentation of Bartter syndrome should be tested using R198 Renal tubulopathies

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation, after exclusion of acquired causes

Requesting Specialties

- Clinical Genetics
- Endocrinology
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R256.1	Nephrocalcinosis or nephrolithiasis WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Nephrocalcinosis or nephrolithiasis (149)	WES or Medium Panel

R256肾钙质沉着症or肾结石

检测标准

肾钙质沉着症或肾结石症，且已排除获得性病因

重叠指征

- 如发现钙稳态的原发性内分泌紊乱，应使用相应的特异性检测
  应使用
- 对于存在可识别原发性肾脏疾病的个体，在适合进行基因检测时应使用针对该疾病的具体检测

- 可能由 Bartter 综合征引起的肾钙质沉着症个体可按此指征进行检测；表现不同的 Bartter 综合征个体应使用 R198 进行检测
  肾小管病

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时，在排除获得性病因后

申请专科

- 临床遗传学
- 内分泌学
- 肾脏科

专科服务组

- 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R256.1	肾钙质沉着症或肾结石 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	肾钙质沉着症或肾结石（149）	WES或Medium检测板

R257 Unexplained young onset end-stage renal disease

Testing Criteria

End-stage renal disease developing under the age of 36, with no identifiable cause detectable by renal biopsy, biochemistry, imaging or clinical assessment

Use of this test in young adults over the age of 36 may be appropriate after expert clinical review, if there is strong clinical suspicion of a monogenic disorder

Overlapping conditions:

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or syndromic presentations

Testing Criteria for Semi-Rapid Testing

- Acutely unwell children or adults where monogenic young onset end-stage renal disease is considered highly likely to be the primary cause of the phenotype in the patient.

- Cases should meet the standard eligibility criteria for R257, AND

- Where testing will provide an immediate change to treatment or clinical management for the patient eg. To inform a decision about renal transplant, therapeutic intervention or prenatal testing for an ongoing at risk pregnancy.

- The patient is either not eligible for the R14 pathway or Rapid R257 is considered to be the more appropriate test.

Where in Pathway

At presentation

Where in Pathway for Semi-Rapid Testing

At presentation following clinically relevant, rapidly available investigations. All cases must be agreed in advance with the testing laboratory.

Requesting Specialties

- Clinical Genetics
- Nephrology

Requesting Specialties for Semi-Rapid Testing

- Clinical Genetics
- Renal
- Neonatology

Specialist Service Group

- Renal

Associated Tests

R257.3 is only for semi urgent testing

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R257.2	Unexplained end-stage renal disease WGS (phase 2)	Trio or singleton	Exon level CNVs, Small variants	Panel of genes or loci	Unexplained end-stage renal disease (678)	WGS
R257.3	Unexplained end-stage renal disease WES	Trio	Small variants	Panel of genes or loci	Unexplained end-stage renal disease (678)	WES

R257不明原因年轻起病终末期肾脏疾病

检测标准

36 岁前发生终末期肾病，且通过肾活检、生化、影像学或临床评估均未发现可识别病因

对于 36 岁以上的年轻成人，如临床强烈怀疑单基因疾病，经专家临床审查后使用该检测可能是适当的。重叠疾病：

• R27 儿科疾病或 R89 超罕见和非典型单基因疾病检测应用于
存在先天性畸形、面容异常或其他复杂或综合征性表现的个体

半快速检测标准

- 急性病情严重的儿童或成人，且认为单基因年轻起病终末期肾病极可能是该患者表型的原发病因。

- 病例应符合 R257 的标准资格标准，并且

- 检测将立即改变患者治疗或临床管理的情况，例如为肾移植决策、治疗干预或对正在进行的风险妊娠进行产前检测提供信息。

- 患者不符合 R14 路径的资格，或认为 Rapid R257 是更适当的检测。

通路中的位置

半快速检测路径中

在临床相关、可快速获得的检查后就诊时。所有病例必须事先与检测实验室达成一致。

• 临床遗传学
• 肾脏科

申请专科进行半快速检测

• 临床遗传学
• 肾脏
• 新生儿科

专科服务组

• 肾脏

相关检测

R257.3仅用于半紧急检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R257.2	不明原因的终末-期肾疾病 WGS (phase 2)	三联体或单例外显	子水平 CNVs，小变异	基因检测板或基因座	不明原因终末期肾病 (678)	全基因组测序
R257.3	不明原因终末期肾疾病 WES	三人组	小变异基因面板	或不明原因终末期基因座	肾病 (678)	全外显子组测序

R446 APOL1 kidney donor testing

Testing Criteria

Testing for potential living donors, where ALL the following criteria are met:

1. The individual is being assessed for living kidney donation AND
2. Both the individual's parents have (or are likely to have) African, African-American, Caribbean or Brazilian heritage AND
3. Individual has undergone counselling and understands the indications and implications of testing and has provided consent.

Where in Pathway

Testing should be performed by transplant specialists after a potential donor has undergone basic biochemical, tissue type and antibody testing but before exposing the donor to ionising radiation e.g. CT renal angiogram.

Requesting Specialties

- Clinical genetics
- Nephrology

Specialist Service Group

- Renal

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R446.1	APOL1 kidney donor testing	Singleton	Targeted variant testing	Single gene	APOL1	Single gene sequencing < 10 amplicons

R446APOL1肾脏供者检测

检测标准

对潜在活体供者进行检测，需满足以下所有标准：

1. 该个体正在接受活体肾脏捐献评估，并且
2. 该个体的父母双方均具有(或很可能具有)非洲、非裔美国人、加勒比或巴西血统 AND
3. 个体已接受咨询并了解检测的指征和意义，且已提供知情同意。

通路中的位置

检测应由移植专科医生在潜在供者完成基本生化、组织分型和抗体检测之后、但在使供者暴露于电离辐射(如 CT 肾血管造影)之前进行。

申请专科

• 临床遗传学
• 肾脏科

专科服务组

• 肾脏

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R446.1	APOL1肾病供体检测	单人	靶向变异检测	单基因	APOL1	单基因测序 < 10扩增子

Part XIX. Respiratory

R184 Cystic fibrosis diagnostic test

Testing Criteria

Test in an individual clinically likely to be affected with cystic fibrosis:

1. Child with clinical suspicion of CF (e.g. recurrent chest infections, failure to thrive, fat malabsorption, neonatal history of meconium ileus), AND
   a. A not normal sweat test performed in a recognised experienced test centre/laboratory (i.e. sweat chloride ≥30mM with sufficient sweat obtained), OR
   b. An additional urgent prenatal situation for the parents or for a close relative, but urgent sweat testing not accessible
2. Adult with CT-proven bronchiectasis, AND
   a. A not normal sweat test performed in a recognised experienced test centre/laboratory (i.e. sweat chloride ≥30mM with sufficient sweat obtained), OR
   b. Chronic suppurative chest infection with colonisation by Pseudomonas and Staph aureus, OR
   c. Additional exocrine pancreatic dysfunction
3. Idiopathic chronic pancreatitis with exocrine dysfunction (fat malabsorption) with other obvious and acquired causes excluded, AND
   a. A not normal sweat test performed in a recognised experienced test centre/laboratory (i.e. sweat chloride ≥30mM with sufficient sweat obtained), OR
   b. Sweat testing not practical, and all other causes excluded
4. Infertility associated with obstructive azoospermia, AND
   a. CBAVD (or isolated CUAVD) diagnosed from expert clinical examination, OR
   b. CBAVD identified at incidental herniotomy
5. Fetal echogenic bowel as bright as bone on 2nd trimester scan or dilated fetal bowel on 2nd or 3rd trimester scan with echogenic bowel as bright as bone, AND
   a. both parents not available for carrier testing [if both parents are available, Cystic fibrosis carrier testing should be used instead of an invasive prenatal test], AND
   b. Other more common causes excluded (e.g. IUGR, placental failure, earlier bleeding, infection, raised aneuploidy markers)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Initial population-specific targeted test sufficient to exclude CF as the likely diagnosis in the absence of a clear clinical diagnosis

Proceed to a full gene test if the targeted test is negative and there is a high clinical suspicion of a diagnosis of Cystic Fibrosis

Requesting Specialties

For R184.1 CFTR Targeted variant testing

- Clinical Genetics
- Fetal Medicine
- Gastroenterology
- Genomics laboratory
- Gynaecology
- Obstetrics
- Paediatrics
- Respiratory Medicine

第XIX部分：呼吸系统

R184囊性纤维化诊断性检测

检测标准

对临床上可能患有囊性纤维化的个体进行检测：

1. 临床怀疑 CF 的儿童(如反复胸部感染、生长发育迟缓、脂肪吸收不良、新生儿胎粪性肠梗阻史),AND
   a. 在公认有经验的检测中心/实验室进行的汗液试验结果不正常(即汗氯 ≥30mM 且获得足量汗液),OR
   b. 父母或近亲存在额外的紧急产前情况，但无法进行紧急汗液检测
2. 成人经CT证实的支气管扩张，且
   a. 在公认有经验的检测中心/实验室进行的汗液试验结果不正常(即汗氯 ≥30mM 且获得足量汗液),OR

   b.慢性化脓性胸部感染，伴铜绿假单胞菌和金黄色葡萄球菌定植，或 c.额外的外分泌胰腺功能障碍
3. 特发性慢性胰腺炎伴外分泌功能障碍(脂肪吸收不良)，已排除其他明显和获得性病因，且 a.在公认的有经验的检测中心/实验室进行的汗液检测结果不正常(即汗液

   氯化物 ≥30mM 且汗液量充足)，或
   b. 汗液检测不可行，且已排除所有其他病因
4. 与梗阻性无精子症相关的不育，且 a.经专家临床检查诊断为CBAVD(或孤立性CUAVD)，或 b. 在偶然的疝切开术中发现的CBAVD
5. 孕中期超声检查发现胎儿肠管回声增强，强度与骨骼相当，或孕中晚期超声检查发现胎儿肠管扩张伴肠管回声增强，强度与骨骼相当，且 a.父母双方均无法进行携带者检测[若父母双方均可进行检测，应使用囊性纤维化携带者检测而非侵入性产前检测]，且 b.已排除其他更常见的原因(如IUGR、胎盘功能不全、早期出血、感染，

   (非整倍体标志物升高)

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在缺乏明确临床诊断的情况下，初始的人群特异性靶向检测足以排除CF作为可能诊断。若靶向检测为阴性且临床高度怀疑囊性纤维化诊断，则继续进行全基因检测。申请专科

对于 R184.1 CFTR 靶向变异检测

- 临床遗传学
- 胎儿医学
- 胃肠病学
- 基因组实验室
- 妇科
- 产科
- 儿科
- 呼吸医学

For R184.2 and R184.3 Single gene sequencing and MLPA

- CF service,
- Clinical Genetics
- Respiratory medicine

Specialist Service Group

- Core

Associated Tests

Please note all the tests below will be undertaken for R184 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

R65 “Aminoglycoside exposure posing risk to hearing” testing will be carried out in any patient with a confirmed diagnosis of Cystic Fibrosis as a result of the R184 test.

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R184.1	CFTR Targeted variant testing	Singleton	Small variants	Single gene(s)	CFTR (1318)	Targeted variant testing
R184.2	CFTR Single gene sequencing	Singleton	Small variants	Single gene(s)	CFTR (1318)	Single gene sequencing >=10 amplicons
R184.3	CFTR MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	CFTR (1318)	MLPA or equivalent

对于 R184.2 和 R184.3 单基因测序和 MLPA

- CF 服务，
- 临床遗传学
- 呼吸内科

专科服务组

- 核心

相关检测

请注意，对于R184临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明并非所有检测都是必要的

R65“氨基糖苷类暴露对听力构成风险”检测将在因R184检测而确诊为囊性纤维化的任何患者中进行。

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R184.1	CFTR靶向变异检测	单人	小变异	单基因	CFTR (1318)	靶向变异检测
R184.2	CFTR单基因测序	单人	小变异	单基因	CFTR (1318)	单基因测序 >=10扩增子
R184.3	CFTR MLPA或等效	单人	外显子水平拷贝数变异	单基因	CFTR (1318)	MLPA或等效

R185 Cystic fibrosis carrier testing

Testing Criteria

1. Prospective egg or sperm donor
2. Family history of CF in close relative (up to 4th degree, i.e. in 1st cousin's child or closer relative), or in a similar close relative of partner
3. Partner of a known CF carrier
4. Close consanguineous couple (1st cousins), AND from an ethnic group with a high carrier frequency
5. Both parents of a fetus with echogenic bowel (where both parents are available)
6. Both parents of a fetus with dilated bowel (where both parents are available)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

R184 Cystic fibrosis diagnostic test should be used where a fetus has echogenic bowel and BOTH parents are not available for testing

Where in Pathway

At time of reproductive planning

Requesting Specialties

- Clinical Genetics
- Fetal Medicine
- Gynaecology
- Respiratory medicine
- General practice

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R185.1	CFTR Targeted variant testing	Singleton	Small variants	Single gene(s)	CFTR	Targeted variant testing

R185囊性纤维化携带者检测

检测标准

1. 预期卵子或精子捐赠者
2. 近亲(至4级，即1代表亲的孩子或更近的亲属)有CF家族史，或伴侣的类似近亲有CF家族史
3. 已知CF携带者的伴侣
4. 近亲婚配夫妇(1代表亲)，且来自携带者频率高的族群
5. 超声回声肠胎儿的双亲(双亲均可提供样本时)
6. 胎儿肠管扩张时其父母双方(父母双方均可获得)

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

当胎儿有肠管回声增强且父母双方均无法进行检测时，应使用R184囊性纤维化诊断检测

通路中的位置

生殖计划时申请专科

• 临床遗传学
• 胎儿医学
• 妇科
• 呼吸内科
• 全科医疗

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R185.1	CFTR靶向变异检测	单人	小变异	单基因	CFTR	靶向变异检测

R253 Cystic fibrosis newborn screening follow-up

Testing Criteria

Positive IRT test on newborn screening, according to definition in the National Standard Protocol for Cystic Fibrosis

Where in Pathway

According to the National Standard Protocol for Cystic Fibrosis

Requesting Specialties

- Appropriate specialist referring clinician

Specialist Service Group

- Screening

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R253.1	CFTR 4 commonest variants Targeted variant testing	Singleton	Small variants	Single interval	CFTR 4 commonest variants	Targeted variant testing

R253囊性纤维化新生儿筛查随访

检测标准

新生儿筛查IRT检测阳性，依据囊性纤维化国家标准方案中的定义

通路中的位置

根据囊性纤维化国家标准化方案

申请专科

• 适当的专科转诊临床医生

专科服务组

• 筛查

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R253.1	CFTR 4 最常见的 变异靶向变异检测	单人	小变异	单一区间	CFTR 4种最常见变异	靶向变异检测

R333 Central congenital hypoventilation

Testing Criteria

Clinical features suggestive of congenital central hypoventilation syndrome:

1. Central alveolar hypoventilation, AND
2. Absence of primary lung, cardiac or neuromuscular cause or identifiable brainstem lesion, WITH OR WITHOUT the following additional PHOX2B-reated features:
   a. Hirschsprung disease, OR
   b. Neuroblastoma or other neural crest tumour, OR
   c. Autonomic dysfunction, for example affecting the cardiovascular system, gastrointestinal tract, sweating or temperature control

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neonatology
- Neurology
- Respiratory Medicine

Specialist Service Group

- Respiratory

Associated Tests

Please note all the tests below will be undertaken for R333 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary.

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R333.1	PHOX2B STR testing	Singleton	STRs	Single gene(s)	PHOX2B (1314)	STR testing
R333.2	PHOX2B Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	PHOX2B (1314)	Single gene sequencing >=10 amplicons

R333中枢性先天性低通气

检测标准

提示先天性中枢性低通气综合征的临床特征：

1. 中枢性肺泡低通气，AND
2. 无原发性肺、心脏或神经肌肉病因或可识别的脑干病变，伴或不伴以下额外的PHOX2B相关特征：
   a. 先天性巨结肠，OR
   b. 神经母细胞瘤或其他神经嵴肿瘤，或
   c. 自主神经功能障碍，例如影响心血管系统、胃肠道、出汗或体温调节

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 新生儿科
• 神经科
• 呼吸医学

专科服务组

• 呼吸系统

相关检测

请注意，对于R333临床指征请求，将进行以下所有检测，除非临床表现和/或初始结果表明并非所有检测都是必要的。

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R333.1	PHOX2B STR 检测	单人	短串联重复序列	单基因	PHOX2B (1314)	短串联重复序列检测
R333.2	PHOX2B单基因测序	单人	小变异，拷贝数变异	单基因	PHOX2B (1314)	单基因测序 >=10扩增子

R139 Laterality disorders and isomerism

Testing Criteria

1. Classical heterotaxy affecting more than one body system, OR
2. Non-classical heterotaxy (an isolated heterotaxy-type malformation), OR
3. Combination of malformations which may occur in heterotaxy but which are not diagnostic of heterotaxy (e.g. oesophageal atresia with intestinal malrotation)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Cardiology
- Clinical Genetics

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R139.1	Laterality disorders and isomerism WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Laterality disorders and isomerism (549)	WES or Medium Panel

R139偏侧性疾病和异构

检测标准

1. 影响多个身体系统的典型异位症，或
2. 非典型异位症(孤立性异位症型畸形)，或
3. 可能发生于内脏异位但不足以诊断内脏异位的畸形组合(如食管闭锁伴肠旋转不良)

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 心脏病学

• 临床遗传学

专科服务组

• 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R139.1	偏侧性障碍和异构现象 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	偏侧性障碍和异构现象 (549)	WES或Medium检测板

R186 Hereditary haemorrhagic telangiectasia

Testing Criteria

Test where any THREE of the following criteria are met:

1. Epistaxis: spontaneous, recurrent nose bleeds
2. Telangiectases: multiple, at characteristic sites (lips, oral cavity, fingers, nose)
3. Visceral lesions such as gastrointestinal telangiectasia (with or without bleeding), pulmonary arteriovenous malformation (AVM), hepatic AVM, cerebral AVMs, spinal AVM
4. Family history: a first degree relative with HHT according to these criteria (as above) or an autosomal dominant family history of nosebleeds or first degree relative with cerebral AVM / cerebral haemorrhage / pulmonary or hepatic AVM.

Alternatively, test where any ONE of the following criteria are met:

A) Personal history of at least one pulmonary AVM*

B) Personal history of two or more AVMs at one or more characteristic sites (pulmonary*, cerebral, hepatic or spinal)

C) Personal history of at least one AVM and severe epistaxis or characteristic telangiectasia or family history

D) Personal history of telangiectasia, and refractory or severe epistaxis (e.g. requiring recurrent transfusions) *

*Pulmonary AVM only if confirmed by cross sectional imaging (usually thoracic CT scan), and/or later therapeutic angiography/surgery. Do not diagnose if only supported by a positive right-to-left shunt study ("bubble echo") or chest x-ray.

To Note: if there is no antecedent family history implying a "first in family" case more likely to be mosaic.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Gastroenterology
- Neurology
- Respiratory Medicine

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R186.1	Hereditary haemorrhagic telangiectasia Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Hereditary haemorrhagic telangiectasia (123)	Small panel

R186遗传性出血性毛细血管扩张症

检测标准

检测以下标准中任意三项均满足的情况：

1. 鼻出血：自发性、反复性鼻出血
2. 毛细血管扩张：多发，位于特征性部位(唇、口腔、手指、鼻)
3. 内脏病变，如胃肠道毛细血管扩张(伴或不伴出血)、肺动静脉畸形(AVM)、肝AVM、脑AVM、脊髓AVM
4. 家族史：根据这些标准(如上)有一级亲属患有HHT，或常染色体显性遗传的鼻出血家族史，或一级亲属患有脑AVM/脑出血/肺或肝AVM。

或者，检测符合以下任一标准的情况：

A) 至少一次肺动脉动静脉畸形(AVM)的个人史*

B) 个人史中有两个或更多AVM位于一个或多个特征性部位(肺*、脑、肝或脊髓)

C) 个人史中至少有一个AVM和严重鼻出血或特征性毛细血管扩张或家族史

D) 个人史中有毛细血管扩张，以及难治性或严重鼻出血(如需要反复*肺AVM仅在经横断面成像(通常为胸部CT扫描)和/或后续治疗性血管造影/手术确认时。若仅由阳性右向左分流研究("气泡超声")或胸部X线支持，则不应诊断。输血)*

注意：若无提示"家族首例"的既往家族史，则更可能为嵌合体。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 皮肤病学
- 胃肠病学
- 神经科
- 呼吸医学

专科服务组

- 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R186.1	遗传性出血性毛细血管扩张症小 panel	单人	小变异，拷贝数变异	基因检测板或基因座	遗传性出血性毛细血管扩张症 (123)	小检测板

R188 Pulmonary arterial hypertension

Testing Criteria

Idiopathic PAH or suspected Familial/Heritable Pulmonary Arterial Hypertension (PAH).

Overlapping indications

- R186 Hereditary haemorrhagic telangiectasia test should be used in patients with PAH and HHT

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Respiratory Medicine

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R188.1	Pulmonary arterial hypertension Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Pulmonary arterial hypertension (193)	Small panel

R188肺动脉高压

检测标准

特发性PAH或疑似家族性/遗传性肺动脉高压(PAH)。

重叠指征

• R186 遗传性出血性毛细血管扩张症检测应用于PAH合并HHT的患者

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 呼吸医学

专科服务组

• 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R188.1	肺动脉高血压 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	肺动脉高压 (193)	小检测板

R189 Respiratory ciliopathies including non-CF bronchiectasis

Testing Criteria

1. Neonatal presentation with at least one of:
   a. Situs inversus plus lower airway or nasal symptoms, OR
   b. Persistent respiratory distress where other causes have been excluded, OR
   c. Persistent rhinorrhea and cough where other causes have been excluded, OR
2. Testing in childhood with at least one of:
   a. Persistent life-long wet cough (CF excluded)
   b. Unexplained bronchiectasis (CF excluded)
   c. Serous otitis media in association with lower and upper airway symptoms
3. Testing in adults who have had symptoms as above since early childhood, often associated with infertility or subfertility

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Respiratory Medicine

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R189.1	Respiratory ciliopathies including non-CF bronchiectasis WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Respiratory ciliopathies including non-CF bronchiectasis (550)	WES or Medium Panel

R189呼吸系统纤毛病包括非CF支气管扩张

检测标准

1. 新生儿期表现，至少具备以下一项：
   a. 内脏反位加下呼吸道或鼻部症状，或
   b.持续性呼吸窘迫且已排除其他病因，或 c.持续性鼻漏和咳嗽且已排除其他病因，或
2. 儿童期检测，至少满足以下一项：
   a.持续性终生湿性咳嗽(已排除CF) b.不明原因的支气管扩张(已排除CF) c.浆液性中耳炎伴下呼吸道和上呼吸道症状
3. 对自幼儿期起即有上述症状的成人进行检测，常伴有不育或生育力低下

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 呼吸医学

专科服务组

• 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R189.1	呼吸系统纤毛病 包括非CF支气管扩张 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	呼吸系统纤毛病包括非囊性纤维化支气管扩张（550）	WES或Medium检测板

R190 Pneumothorax – familial

Testing Criteria

1. Primary spontaneous pneumothorax with no identifiable cause AND a first degree relative with primary spontaneous pneumothorax,

OR

2. Characteristic radiological features of Birt-Hogg-Dubé syndrome on chest imaging

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Respiratory Medicine

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R190.1	Pneumothorax – familial Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Pneumothorax – familial (105)	Small panel

R190气胸-家族性

检测标准

1. 原发性自发性气胸且无可识别病因，并且有一名患原发性自发性气胸的一级亲属，或

2. 胸部影像学显示Birt-Hogg-Dubé综合征的特征性放射学表现

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 呼吸医学

专科服务组

• 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R190.1	气胸 – 家族性小检测板	单人	小变异，拷贝数变异	基因检测板或基因座	气胸 – 家族性（105）	小检测板

R191 Alpha-1-antitrypsin deficiency

Testing Criteria

Plasma concentration of alpha-1-antitrypsin below normal range, AND

1. Prolonged neonatal jaundice with an inconclusive alpha-1-antitrypsin phenotyping result, OR
2. Variant analysis will inform reproductive choice, OR
3. Adult with cirrhosis or emphysema where a genetic diagnosis would influence management following an inconclusive alpha-1-antitrypsin phenotyping result

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

In most patients, an alpha-1-antitrypsin phenotyping test will be sufficient to establish the diagnosis

Genetic testing can be used for diagnostic confirmation in the situations specified in the Eligibility Criteria

Cascade testing of relatives is rarely indicated.

Requesting Specialties

- Clinical Genetics
- Gastroenterology
- Hepatology
- Respiratory Medicine
- General practice

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R191.1	SERPINA1 common variants Targeted variant testing	Singleton	Small variants	Single interval	SERPINA1 common variants	Targeted variant testing

R191α1-抗胰蛋白酶缺乏症

检测标准

α-1-抗胰蛋白酶血浆浓度低于正常范围，且

1. 新生儿迁延性黄疸伴α-1-抗胰蛋白酶表型分析结果不确定，或
2. 变异分析将为生殖选择提供依据，或
3. 患有肝硬化或肺气肿的成人，在α-1-抗胰蛋白酶表型分析结果不确定后，基因诊断将影响管理

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在大多数患者中，α-1-抗胰蛋白酶表型检测足以确立诊断

基因检测可用于检测资格标准中所规定情形下的诊断确认。亲属的级联检测很少适用。

- 临床遗传学
- 胃肠病学
- 肝脏病学
- 呼吸医学
- 全科医疗

专科服务组

- 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R191.1	SERPINA1 常见变异 靶向变异 检测	单人	小变异	单一区间	SERPINA1常见变异	靶向变异检测

R462 Childhood interstitial lung disease

Testing Criteria

Hypoxia not sufficiently explained by an alternative diagnosis

AND

Computed tomography (CT), reviewed by specialist chest radiologist and respiratory paediatrician suggestive of childhood interstitial lung disease. Unless patient too unwell for chest CT, for example on extra-corporeal life support.

Corrected gestational age 37 weeks or older

Where in Pathway

At presentation

Requesting Specialties

- Paediatric respiratory medicine

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R462.1	Childhood interstitial lung disease	Singleton	SNVs, CNVs	Panel of genes or loci	SFTPA1, TERT , PARN, STAT1, FLNA, SFTPA2, TERC, TINF2, STAT5B, FOXF1, SFTPB, NAF1, COPA, TMEM173, ITGA3, SFTPC, MARS1, PSMB4, SLC34A2, CSF2RA, ABCA3, RTEL1, PSMB8, BMPR2, CSF2RB, NKX2-1 (TTF-1), OAS1, PSMB9, TBX4, RAB5B (amber), GATA2, SLC7A7, LRBA, FARSA, FARSB Childhood interstitial lung disease (1638)	Medium panel

R462儿童期间质性肺疾病

检测标准

缺氧不能由其他诊断充分解释

和

计算机断层扫描(CT)，由专科胸部放射科医师和呼吸儿科医师审阅，提示儿童期间质性肺疾病。除非患者病情过重无法进行胸部CT，例如正在接受体外生命支持。

纠正胎龄37周或以上

通路中的位置

就诊时

申请专科

• 儿科呼吸医学

专科服务组

• 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R462.1	儿童期间质性肺病	单人	SNVs、CNVs	基因检测板或基因座	SFTPA1、TERT、PARN、STAT1 FLNA、SFTPA2、TERC、TINF2、STAT5B、FOXF1、SFTPB、NAF1, COPA, TMEM173, ITGA3, SFTPC, MARS1, PSMB4, SLC34A2, CSF2RA, ABCA3, RTEL1, PSMB8, BMPR2, CSF2RB, NKX2-1 (TTF-1), OAS1, PSMB9, TBX4, RAB5B (琥珀色), GATA2, SLC7A7, LRBA, FARSA, FARSB 儿童间质性肺病(1638)	中检测板

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R330 Alveolar capillary dysplasia with misalignment of pulmonary veins

Testing Criteria

1. Respiratory distress and severe pulmonary hypertension presenting within the first two days of life, and without any sustained response to supportive measures, AND
2. Additional malformations affecting cardiac, gastrointestinal and genitourinary systems

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Neonatology
- Respiratory Medicine

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R330.1	FOXF1 Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	FOXF1 (1211)	Single gene sequencing >=10 amplicons

R330肺泡毛细血管发育不良伴排列异常的肺静脉

检测标准

1. 在出生后最初两天内出现呼吸窘迫和重度肺动脉高压，并且在采取支持性措施后仍无任何持续反应，且
2. 影响心脏、胃肠道和泌尿生殖系统的额外畸形

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 新生儿科
- 呼吸医学

专科服务组

- 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R330.1	FOXF1单基因测序	单人	小变异，拷贝数变异	单基因	FOXF1 (1211)	单基因测序 >=10扩增子

R421 Pulmonary Fibrosis Familial

Testing Criteria

Interstitial Lung Disease (ILD) and **ONE** of the following:

1. ILD, no identifiable cause or association, and age <50 years.
2. Family history of ILD regardless of identifiable cause or association
3. For suspected telomerase complex variants, testing to be considered in the absence of 1. and 2. above if one or more of the following are present in addition to ILD:
   - unexplained haematological abnormalities including macrocytosis, anaemia, thrombocytopenia, leukopenia and/or isolated lymphopenia;
   - unexplained haematological abnormalities including macrocytosis, anaemia, thrombocytopenia, leukopenia and/or isolated lymphopenia; premature greying,
   - or unexplained liver function abnormalities.
   - Consideration of lung transplantation

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Respiratory Medicine
- Haematology
- Hepatology

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R421.1	Pulmonary Fibrosis Familial	Singleton	Small variants, CNVs	Panel of genes or loci	Medium panel to be created in PanelApp	WES or medium panel

R421肺纤维化家族性检测标准

间质性肺疾病(ILD)及以下各项之一：

1. ILD，无可识别的原因或关联，且年龄<50岁。
2. 无论病因或关联是否明确，ILD家族史
3. 对于疑似端粒酶复合物变异，若除ILD外还存在以下一项或多项，且不存在上述1.和2.的情况，应考虑检测：
   - 不明原因的血液学异常，包括大细胞增多症、贫血、血小板减少症，白细胞减少和/或孤立性淋巴细胞减少；
   - 不明原因的血液学异常，包括大细胞增多症、贫血、血小板减少症，白细胞减少和/或孤立性淋巴细胞减少；过早白发，
   - 或不明原因的肝功能异常。
   - 考虑肺移植

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 呼吸医学
- 血液学
- 肝脏病学

专科服务组

- 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R421.1	肺纤维化家族性	单人	小变异，拷贝数变异	基因检测板或基因座	中检测板将在PanelApp	WES或中等检测组合

R426 Pulmonary alveolar microlithiasis

Testing Criteria

Individuals with a clinical suspicion/diagnosis of PAM including presence of diffuse intra-alveolar microliths, typically with widespread nodular calcification, on chest imaging.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Genomic laboratory
- Respiratory medicine

Specialist Service Group

- Respiratory

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R426.1	Pulmonary alveolar microlithiasis Single gene sequencing	Singleton	Small variants, CNVs	Single gene(s)	SLC34A2 (1383)	Single gene sequencing >=10 amplicons

R426肺泡微结石症

检测标准

临床怀疑/诊断为PAM的个体，包括胸部影像学显示弥漫性肺泡内微结石，通常伴有广泛的结节状钙化。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

- 临床遗传学
- 基因组实验室
- 呼吸内科

专科服务组

- 呼吸系统

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R426.1	肺 肺泡 微结石症 单基因 测序	单人	小变异， 拷贝数变异	单基因	SLC34A2 (1383)	单基因测序 ≥10个扩增子

Part XX. Dermatology

R110 Segmental overgrowth disorders – Deep sequencing

Testing Criteria

Clinical features suggestive of a segmental overgrowth disorder. Features may include:

1. Congenital or early onset segmental overgrowth (which may affect the brain only, i.e. megalencephaly)
2. Confirmed Vascular malformations (capillary, venous, lymphatic or combinations) following discussion with a specialist
3. Characteristic cutaneous features (for example epidermal naevi or connective tissue naevi)
4. Brain malformations (for example hydrocephalus or cortical malformations)
5. Additional dysmorphism (for example polydactyly)

Overlapping indications

- R27 Paediatric disorders or R89 Ultra-rare and atypical monogenic disorders tests should be considered in overlapping features are present but germline variant is considered likely

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

NOTE: Many of these disorders are anticipated to be mosaic and sample type and test technology must take account of this. An assay capable of detecting mosaicism below 10% should be used, e.g high read depth sequencing and an appropriate bioinformatic pipeline.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Surgery*

*plastic

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R110.1	Segmental overgrowth disorders – Deep sequencing Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Segmental overgrowth disorders – Deep sequencing (98)	Small panel

第XX部分：皮肤病学

R110节段性过度生长疾病-深度测序

检测标准

临床特征提示节段性过度生长疾病。特征可能包括：

1. 先天性或早发性节段性过度生长(可能仅影响大脑，即巨脑症)
2. 经与专科医师讨论后确认的血管畸形(毛细血管、静脉、淋巴管或组合)
3. 特征性皮肤表现(例如表皮痣或结缔组织痣)
4. 脑畸形(例如脑积水或皮质畸形)
5. 其他畸形特征(例如多指畸形)

重叠指征

• 应考虑R27儿童期疾病或R89超罕见和非典型单基因疾病检测
当存在重叠特征但胚系变异被认为可能

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

注意：预计其中许多疾病为嵌合性，样本类型和检测技术必须考虑到这一点。应使用能够检测低于10%嵌合现象的测定方法，例如高读取深度测序和适当的生物信息学流程。

通路中的位置

申请专科

• 临床遗传学
• 皮肤病学
• 手术*

*塑料

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R110.1	节段性过度生长疾病 - 深度测序小	单人	小变异，拷贝数变异	基因检测板或基因座	节段性过度生长障碍 – 深度测序 (98)	小检测板

R163 Ectodermal dysplasia

Testing Criteria

Individuals with a clinical diagnosis of ectodermal dysplasia who have one or more of:

1. Abnormalities of hair (hypotrichosis, sparse hair, sparse/missing eyebrows)
2. Abnormalities of teeth (hypodontia, conical incisors)
3. Abnormalities of skin (hypohidrosis, episodes of hyperthermia)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Surgical Dentistry

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R163.1	Ectodermal dysplasia WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Ectodermal dysplasia (553)	WES or Medium panel

R163外胚层发育不良

检测标准

临床诊断为外胚层发育不良的个体，且具有以下一项或多项：

1. 毛发异常(毛发稀少、头发稀疏、眉毛稀疏/缺失)
2. 牙齿异常(缺牙、锥形切牙)
3. 皮肤异常(少汗、高热发作)

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 皮肤病学
• 口腔外科

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R163.1	外胚层发育不良 WES 或中等 Panel	单人	小变异，拷贝数变异	基因检测板或基因座	外胚层发育不良 (553)	WES或Medium检测组合

R164 Epidermolysis bullosa and congenital skin fragility

Testing Criteria

Individuals with a clinical diagnosis of epidermolysis bullosa or other forms of unexplained skin fragility including peeling skin syndrome

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

For most patients, the test will be arranged as part of assessment in the highly specialised epidermolysis bullosa service

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R164.1	Epidermolysis bullosa and congenital skin fragility WES or medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Epidermolysis bullosa and congenital skin fragility (554)	WES or Medium Panel

R164大疱性表皮松解症及先天性皮肤脆性

检测标准

临床诊断为大疱性表皮松解症或其他不明原因皮肤脆性增加(包括剥脱性皮肤综合征)的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

对于大多数患者，该检测将作为高度专业化大疱性表皮松解症服务评估的一部分进行安排

申请专科

• 临床遗传学

• 皮肤病学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R164.1	表皮松解大疱性和先天性皮肤脆性 WES 或中通量面板	单人	小变异，拷贝数变异	基因检测板或基因座	大疱性表皮松解症和先天性皮肤脆弱 (554)	WES或Medium检测板

R165 Ichthyosis and erythrokeratoderma

Testing Criteria

Individuals with at least TWO features from the list below:

1. Born with collodion membrane
2. Erythroderma
3. Dark plate-like scales or fine white scaling
4. Ectropium/eclabium
5. Hyperkeratosis

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Neonatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R165.1	Ichthyosis and erythrokeratoderma WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Ichthyosis and erythrokeratoderma (555)	WES or Medium panel

R165鱼鳞病和红斑角化病

检测标准

具有以下列表中至少两项特征的个体：1. 出生时伴有胶棉膜

2. 红皮病
3. 深色板状鳞屑或细小白鳞屑
4. 睑外翻/唇外翻
5. 角化过度

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学
• 皮肤病学
• 新生儿科

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R165.1	鱼鳞病和红斑角化病 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	鱼鳞病和红斑角化病 (555)	WES或Medium检测组合

R166 Palmoplantar keratodermas

Testing Criteria

Individuals with unexplained isolated or syndromic keratodermas, including those occurring as part of generalised skin disease.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R166.1	Palmoplantar keratodermas WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Palmoplantar keratodermas (556)	WES or Medium panel

R166掌跖角化病

检测标准

患有不明的孤立性或综合征性角化病(包括作为全身性皮肤病一部分出现的角化病)的个体。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 皮肤病学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R166.1	掌跖角化病 WES或中检测板	单人	小变异，拷贝数变异	基因检测板或基因座	掌跖角化病 (556)	WES或Medium检测组合

R167 Autosomal recessive primary hypertrophic osteoarthropathy

Testing Criteria

Individuals with unexplained digital clubbing, AND either periostosis OR pachydermia

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Respiratory Medicine
- Rheumatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R167.1	Autosomal recessive primary hypertrophic osteoarthropathy Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Autosomal recessive primary hypertrophic osteoarthropathy (557)	Small panel

R167常染色体隐性原发性肥厚性骨关节病

检测标准

患有不明的杵状指，且伴有骨膜增生或厚皮症的个体

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 皮肤病学

• 呼吸医学

• 风湿病学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R167.1	常染色体隐性原发性肥厚性骨关节病小panel	单人	小变异，拷贝数变异	基因检测板或基因座	常染色体隐性原发性肥厚性骨关节病(557)	小检测板

R227 Xeroderma pigmentosum, Trichothiodystrophy or Cockayne syndrome

Testing Criteria

1. Confident clinical diagnosis of xeroderma pigmentosum plus specific XP-related features in the eye, neurological system or a related cancer, OR
2. Confident clinical diagnosis of trichothiodystrophy, OR
3. Confident clinical diagnosis of Cockayne syndrome

Overlapping indications

- R27 Paediatric disorders or
- R89 Ultra-rare and atypical monogenic disorders tests should be used in individuals with congenital malformations, dysmorphism or other complex or less recognisable presentations

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Skin biopsy for complementation testing (specialist DNA repair test) is likely to be required in many patients to confirm the results of the panel test; this can be carried out in parallel with or after the genetic panel test, usually as part of assessment in the Highly Specialised service for xeroderma pigmentosum.

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Please note that the following tests below will be undertaken for R227 dependent on the clinical presentation and/or initial results.

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R227.1	Xeroderma pigmentosum, Trichothiodystrophy or Cockayne syndrome Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Xeroderma pigmentosum, Trichothiodystrophy or Cockayne syndrome (77)	Small panel
R227.2	Genomewide DNA repair defect testing	Singleton	DNA repair	Genomewide	Genomewide	DNA repair defect testing

R227Xeroderma色素性干皮病、毛发硫营养不良或Cockayne综合征

检测标准

1. 明确临床诊断为着色性干皮病，并伴有眼部、神经系统或相关癌症的特异性XP相关特征，或
2. 对毛发硫营养不良的明确临床诊断，或
3. Cockayne 综合征的明确临床诊断

重叠指征

• R27 儿科疾病或

• R89 超罕见和非典型单基因疾病检测应用于患有先天性畸形、形态异常或其他复杂或不易识别的表现

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

许多患者可能需要通过皮肤活检进行互补测试(专门的DNA修复测试)以确认panel检测的结果；这可以与基因panel检测同时或之后进行，通常作为高度专业化着色性干皮病服务评估的一部分。

申请专科

• 临床遗传学

• 皮肤病学

专科服务组

• 皮肤病学

相关检测

请注意，以下针对 R227 的检测将根据临床表现和/或

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R227.1	着色性干皮病色素沉着，毛发硫营养不良 或 Cockayne综合征小panel	单人	小检测板变异，拷贝数变异	着色性干皮病基因或基因座检测组合，	毛发硫营养不良或科凯恩综合征 (77)	小检测板
R227.2	全基因组范围DNA修复缺陷检测	单人	DNA修复	全基因组范围	全基因组范围	DNA修复缺陷检测

R230 Multiple monogenic benign skin tumours

Testing Criteria

Three or more benign skin tumours suggesting a diagnosis of any of the following conditions, with at least two histologically confirmed:

1. Familial cylindromatosis, OR
2. Brooke-Spiegler syndrome, OR
3. Multiple Familial Trichoepithelioma, OR
4. Muir-Torre syndrome, OR
5. Buschke-Ollendorff syndrome*, OR
6. Birt-Hogg-Dubé syndrome

*One skin biopsy may be sufficient to make a confident diagnosis

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R230.1	Multiple monogenic benign skin tumours Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Multiple monogenic benign skin tumours (558)	Small panel

R230多发性单基因良性皮肤肿瘤

检测标准

三个或更多良性皮肤肿瘤提示以下任一情况的诊断，其中至少两个经组织学确认：

1. 家族性圆柱瘤，或
2. Brooke-Spiegler 综合征，OR
3. 多发性家族性毛发上皮瘤，或
4. Muir-Torre 综合征，或
5. Buschke-Ollendorff 综合征*,OR
6. Birt-Hogg-Dubé 综合征

* 皮肤活检可能足以做出明确诊断

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 皮肤病学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R230.1	多种单基因良性皮肤肿瘤小panel	单人	小变异，拷贝数变异	基因检测板或基因座	多种单基因良性皮肤肿瘤 (558)	小检测板

R236 Pigmentary skin disorders

Testing Criteria

1. Multiple café-au-lait macules where neurofibromatosis type 1 (NF1) has been excluded either clinically or on genetic testing, OR
2. Poikiloderma with a likely genetic cause, OR
3. Other forms of reticulate, patchy or speckled hypo- or hyperpigmentation with a likely genetic cause

Overlapping indications

- R222 Neurofibromatosis type 1 test should be used where features are typical of this condition
- R343 Chromosomal mosaicism – microarray test should be used where this is the likely diagnosis
- R327 Mosaic skin disorders – deep sequencing test should be used where the likely cause is a mosaic genetic change, as the technology applied to the mosaic disorders will be more sensitive to these than the panel test designed to detect germline disorders

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Please note all the tests below will be undertaken for R236 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R236.1	Pigmentary skin disorders WES or Large panel	Singleton	Small variants	Panel of genes or loci	Pigmentary skin disorders (559)	WES or Large panel
R236.2	SPRED1 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	SPRED1	MLPA or equivalent

R236色素性皮肤疾病

检测标准

1. 多发性咖啡牛奶斑，且1型神经纤维瘤病(NF1)已在临床上或通过基因检测排除，或
2. 疑似遗传原因的皮肤异色病，或
3. 其他形式的网状、斑片状或斑点状色素减退或色素沉着，具有可能的遗传原因

重叠指征

- R222 1型神经纤维瘤病检测应在特征为该疾病典型表现时使用
- R343 染色体嵌合现象 - 当这可能是诊断时，应使用微阵列(基因芯片)检测
- R327 嵌合性皮肤疾病 - 当可能原因是嵌合性遗传改变时，应使用深度测序检测，因为应用于嵌合性疾病的技术对这些改变比设计用于检测胚系疾病的panel检测更敏感

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 皮肤病学

专科服务组

- 皮肤病学

相关检测

请注意，以下所有检测将针对R236临床指征请求进行，除非临床表现和/或初步结果表明所有检测均不必要

	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R236.1	色素性皮肤疾病 WES 或大 panel	单人	小变异	基因检测板或基因座	色素性皮肤病(559)WES或大	检测组合
R236.2	SPRED1 MLPA或等效	单人	外显子水平拷贝数变异	单基因	SPRED1	MLPA或等效

R237 Cutaneous photosensitivity with a likely genetic cause

Testing Criteria

Clinical diagnosis of a genetic condition causing cutaneous photosensitivity, for example Rothmund-Thompson syndrome, hydroa vacciniforme

Overlapping indications

- Porphyria (cutaneous presentation, R168 or R170) should be tested using the appropriate porphyria test
- R227 Xeroderma pigmentosum, Trichothiodystrophy or Cockayne syndrome test should be used where there is a high likelihood that this is the diagnosis

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R237.1	Cutaneous photosensitivity with a likely genetic cause Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Cutaneous photosensitivity with a likely genetic cause (560)	Small panel

R237皮肤光敏性伴可能遗传病因

检测标准

导致皮肤光敏性的遗传病的临床诊断，例如Rothmund-Thompson综合征、种痘样水疱病

重叠指征

- 卟啉病(皮肤表现，R168或R170)应使用相应的卟啉病检测进行检测
- 在以下情况下应使用R227着色性干皮病、毛发硫营养不良或Cockayne综合征检测
  这很可能是诊断结果

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 皮肤病学

专科服务组

- 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R237.1	皮肤型光敏性伴可能为遗传性原因小 panel	单人	小变异，拷贝数变异	基因检测板或基因座	皮肤光敏性伴可能的遗传原因 (560)	小检测板

R239 Incontinentia pigmenti

Testing Criteria

Confident clinical diagnosis of incontinentia pigmenti or IKBKG-related immunodeficiency.

Overlapping indications

- If the presentation is not specific to incontinentia pigmenti or IKBKG-related immunodeficiency, please use one of the broader tests, for example R15 Primary immunodeficiency or monogenic inflammatory bowel disease, R165 Ichthyosis and erythrokeratoderma, R163 Ectodermal dysplasia or R236 Pigmentary skin disorders tests

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Neonatology
- Neurology
- Ophthalmology
- Immunology (+/- Paediatrics)

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R239.1	IKBKG Single gene sequencing	Singleton	Small variants	Single gene(s)	IKBKG (1347)	Single gene sequencing >=10 amplicons
R239.2	IKBKG common deletion	Singleton	CNVs	Common deletion	IKBKG (1347)	Targeted variant testing

R239色素失禁症

检测标准

色素失禁症或IKBKG相关免疫缺陷的明确临床诊断。

重叠指征

- 如果表现不特异于色素失禁症或IKBKG相关免疫缺陷，请使用更广泛的检测之一，例如R15原发性免疫缺陷或单基因炎症性肠病、R165鱼鳞病和红角化病、R163外胚层发育不良或R236色素性皮肤疾病检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

- 临床遗传学
- 皮肤病学
- 新生儿科
- 神经科
- 眼科
- 免疫学(+/- 儿科)

专科服务组

- 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R239.1	IKBKG单基因测序	单人	小变异	单基因	IKBKG (1347)	单基因测序 >=10扩增子
R239.2	IKBKG常见缺失	单人	拷贝数变异	常见缺失	IKBKG (1347)	靶向变异检测

R255 Epidermodysplasia verruciformis

Testing Criteria

Severe widespread infection with human papillomavirus in the absence of detectable immunodeficiency, with or without squamous cell carcinoma

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R255.1	Epidermodysplasia verruciformis Small panel	Singleton	Small variants, CNVs	Panel of genes or loci	Epidermodysplasia verruciformis (562)	Small panel

R255疣状表皮发育不良

检测标准

在无可检测到的免疫缺陷的情况下，伴或不伴鳞状细胞癌的严重广泛性人乳头瘤病毒感染

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学

• 皮肤病学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R255.1	表皮发育不良疣状 小检测组合	单人	小变异，拷贝数变异	基因检测板或基因座	疣状表皮发育不良 (562)	小检测板

R326 Vascular skin disorders

Testing Criteria

Vascular skin disorders with a likely germline genetic cause

Overlapping indications

- R327 Mosaic skin disorders – deep sequencing test should be used where a mosaic cause is likely, as the technology used for this test will be more sensitive to detect mosaicism
- R110 Segmental overgrowth disorders test should be used where relevant

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R326.1	Vascular skin disorders WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Vascular skin disorders (563)	WES or Medium panel

R326血管性皮肤疾病

检测标准

具有可能种系遗传原因的血管性皮肤疾病

重叠指征

• 在可能为嵌合病因的情况下，应使用R327嵌合性皮肤疾病-深度测序检测，因为该检测所用技术对嵌合现象的检测更为敏感 • 在相关情况下应使用R110节段性过度生长障碍检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

• 皮肤病学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R326.1	血管性皮肤疾病 WES 或中等 Panel	单人	小变异，拷贝数变异	基因检测板或基因座	血管性皮肤疾病 (563)	WES或Medium检测组合

R327 Mosaic skin disorders – deep sequencing

Testing Criteria

Dermatological abnormality likely to have a mosaic single gene cause

Overlapping indications

- R110 Segmental overgrowth disorders test should be used where relevant
- R343 Chromosomal mosaicism – microarray test should be used where a microarray is required

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

NOTE: Many of these disorders are anticipated to be mosaic and sample type and test technology need to take account of this e.g. in planning coverage of NGS assay

Testing for McCune-Albright syndrome is eligible under this clinical indication – appropriate sample type (e.g. diseased tissue) should be considered for this phenotype

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R327.1	Mosaic skin disorders – deep sequencing Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Mosaic skin disorders – deep sequencing (564)	Medium panel

R327嵌合性皮肤疾病-深度测序

检测标准

可能由嵌合型单基因病因导致的皮肤异常

重叠指征

• 在相关情况下应使用 R110 节段性过度生长障碍检测

• 在需要微阵列的情况下，应使用R343染色体嵌合现象-微阵列(基因芯片)检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

注：预计其中许多疾病为嵌合性，样本类型和检测技术需考虑到这一点，例如在规划NGS检测的覆盖范围时

McCune-Albright综合征的检测符合本临床指征的条件--针对该表型应考虑适当的样本类型(例如病变组织)

通路中的位置

申请专科

• 临床遗传学

• 皮肤病学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R327.1	嵌合性皮肤疾病 – 深层测序 中等 Panel	单人	小变异，拷贝数变异	基因检测板或基因座	嵌合性皮肤疾病 – 深层测序 (564)	中检测板

R332 Rare genetic inflammatory skin disorders

Testing Criteria

Clinical diagnosis of a rare inflammatory skin disorder of probably genetic origin, including autoinflammatory disease (e.g. early onset urticaria, recurrent febrile erythemas), infantile pustular psoriasis, likely genetic forms of pityriasis rubra pilaris

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Rheumatology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R332.1	Rare genetic inflammatory skin disorders WES or Medium panel	Singleton	Small variants, CNVs	Panel of genes or loci	Rare genetic inflammatory skin disorders (565)	WES or Medium panel

R332罕见遗传性炎症性皮肤疾病

检测标准

可能为遗传性起源的罕见炎症性皮肤病的临床诊断，包括自身炎症性疾病(例如早发性荨麻疹、复发性发热性红斑)、婴儿期脓疱性银屑病、可能为遗传性形式的毛发红糠疹

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学
• 皮肤病学
• 风湿病学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R332.1	罕见遗传性炎症性皮肤疾病WES或中检测	单人	小变异，拷贝数变异	基因检测板或基因座	罕见遗传性炎症性皮肤疾病 (565)	WES或Medium检测组合

R424 Subcutaneous panniculitis T-cell lymphoma (SPTCL)

Testing Criteria

1. New diagnosis of SPTCL (to guide therapeutic management)
2. Suspected SPTCL (to aid diagnosis)

Detection of the germline HAVCR2 variant is associated with the life-threatening complication of haemophagocytic lymphohistiocytosis (HLH) in a subset of SPTCL patients and also indicates which patients may benefit from immunosuppressive therapy (eg Cyclosporin) as opposed to chemotherapy

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Oncology

Specialist Service Group

- Dermatology

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R424.1	Subcutaneous panniculitis T-cell lymphoma (SPTCL)	Singleton	Small variants	Single gene	HAVCR2 (1394)	Single gene sequencing <=10 amplicons

R424皮下脂膜炎T细胞淋巴瘤(SPTCL)

检测标准

1. 新诊断的SPTCL(用于指导治疗管理)
2. 疑似SPTCL(以辅助诊断)

胚系HAVCR2变异的检出与部分SPTCL患者中危及生命的噬血细胞性淋巴组织细胞增生症(HLH)并发症相关，并且还提示哪些患者可能从免疫抑制治疗(如环孢素)而非化疗中获益

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

就诊时

申请专科

• 临床遗传学
• 皮肤病学
• 肿瘤学

专科服务组

• 皮肤病学

相关检测

代码	名称	最佳家族结构	范围	目标类型	目标名称	方法
R424.1	皮下脂膜炎T细胞淋巴瘤（SPTCL）	单人	小检测板变异	单基因	HAVCR2 (1394)	单基因测序 <=10 扩增子

Part XXI. Ultra-rare and atypical monogenic disorders

R89 Ultra-rare and atypical monogenic disorders

Testing Criteria

- This clinical indication should be used for patients with ultra-rare disorders or atypical manifestations of recognised monogenic disorders that make broad analysis of multiple gene panels that potentially cross different clinical indications the optimal approach. (e.g. for patients where two or more potential genetic disorders are suspected and the patient is eligible for more than one non-WGS test, WGS via R89 could be used).

- **R89 should not be used if appropriate testing is available via another single test in the test directory** (e.g. if testing for monogenic hearing loss only is required this should be requested by the test available for R67).

- **If the patient meets the eligibility criteria for another WGS clinical indication then that indication should be requested as the primary reason for referral but additional panels can be requested, as appropriate,** (e.g. R27 Paediatric disorders).

- Gene panels must be selected for clinical indication R89. These should be entered into the 'Additional panel(s)' box on the WGS test order form.

Requests that include any panel for inherited cancers must be taken to the UKCGG/CanGene-CanVar National Multidisciplinary team meeting and receive delegate approval to proceed.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R89.3	Relevant panels in PanelApp WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Relevant panel(s) in PanelApp	WGS

第XXI.超罕见和非典型单基因疾病

R89超罕见和非典型单基因疾病

检测标准

• 本临床指征应用于患有超罕见疾病或已知单基因疾病非典型表现的患者，这些情况使得对可能跨越不同临床指征的多个基因panel进行广泛分析成为最佳方法。(例如，对于怀疑有两种或多种潜在遗传病且患者符合一种以上非WGS检测条件的患者，可通过R89使用WGS)。

• **如果可通过检测目录中的另一项单一检测获得适当检测，则不应使用R89**(例如，如果仅需要进行单基因听力损失检测，则应通过R67可用的检测进行申请)。

• **如果患者符合另一项WGS临床指征的检测资格标准，则应将该指征作为转诊的主要理由进行申请，但可根据情况申请额外的panel,**(例如R27儿科疾病)。

• 必须为临床指征R89选择基因panel。这些应填入WGS检测申请单上的"附加panel"栏中。

包含任何遗传性癌症panel的申请必须提交至UKCGG/CanGene-CanVar全国多学科团队会议并获得代表批准后方可继续进行。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

申请专科

• 临床遗传学

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R89.3	相关检测组合位于PanelApp全基因组测序（第一阶段）	三人组或单人	外显子水平CNVs，小变异，短串联重复序	基因检测板或基因座	PanelApp中的相关检测组合	全基因组测序

Part XXII. Multi-purpose tests

R240 Diagnostic testing for known variant(s)

Testing Criteria

1. Patient clinically affected with specific disorder where:
   a. the familial variant(s) have already been identified in a relative, OR
   b. there is a recurrent variant for the disorder that is likely to be causative, OR
   c. there is a founder variant for the disorder that is likely to be causative, OR
   d. a variant has been identified in the patient during somatic testing that is likely to be germline origin and causative
2. Molecular confirmation of the diagnosis is required to guide management

This indication is relevant for prenatal and postnatal diagnosis

Where in Pathway

As dictated by clinical situation

Requesting Specialties

- Clinical Genetics
- Other

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R240.1	Specific target Targeted variant testing	Singleton	Small variants	Single interval	Specific Target	Targeted variant testing

第XXII部分多用途检测

R240针对已知变异的诊断性检测()

检测标准

1. 患者临床受特定疾病影响，其中：
   a. 家族性变异已在亲属中确认，或
   b. 该疾病存在一个可能致病的复发性变异，或
   c. 存在该疾病的奠基者变异，可能为致病原因，或
   d. 在体细胞检测中已在患者中发现可能为胚系起源且致病的变异
2. 需要分子确诊以指导管理

该指征适用于产前和产后诊断

通路中的位置

视临床情况而定

申请专科

- 临床遗传学
- 其他

专科服务组

- 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R240.1	特定靶标靶向变异检测	单人	小变异	单一区间	特定靶标	靶向变异检测

R242 Predictive testing for known familial variant(s)

Testing Criteria

Patient requiring predictive testing for specific disorder where the familial variant(s) have already been identified in a relative

Where in Pathway

As dictated by clinical situation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R242.1	Specific target Targeted variant testing	Singleton	Small variants	Single interval	Specific Target	Targeted variant testing

R242针对已知家族性变异的预测性检测()

检测标准

需要对特定疾病进行预测性检测的患者，其家族性变异已在亲属中被识别

通路中的位置

视临床情况而定

申请专科

• 临床遗传学

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R242.1	特定靶标靶向变异检测	单人	小变异	单一区间	特定靶标	靶向变异检测

R244 Carrier testing for known familial variant(s)

Testing Criteria

Patient requiring carrier testing for specific disorder where the familial variant(s) have already been identified in a relative

The range of specialties who will request this test will depend on the disorder in question

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

As dictated by clinical situation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R244.1	Specific target Targeted variant testing	Singleton	Small variants	Single interval	Specific Target	Targeted variant testing

R244针对已知家族性变异的携带者检测()

检测标准

患者需要进行特定疾病的携带者检测，其家族变异已在亲属中确定

申请该检测的专科范围将取决于所涉及的疾病

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

视临床情况而定

申请专科

• 临床遗传学

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R244.1	特定靶标靶向变异检测	单人	小变异	单一区间	特定靶标	靶向变异检测

R246 Carrier testing at population risk for partners of known carriers of nationally agreed autosomal recessive disorders

Testing Criteria

This Clinical Indication relates to carrier testing in partners of individuals who are affected with, or are known carriers with a family history of, an autosomal recessive condition, where:

- management of a current or future pregnancy would be impacted by the result, and the couple would be eligible either for PGD, or for prenatal diagnosis under the clinical indication R448 Prenatal Testing

or

- carrier testing of a partner is feasible and will inform/determine clinical management (including surveillance) for their children.

This Clinical Indication is not intended to influence decision making, related to reporting of incidental carrier findings in genes associated with autosomal recessive disorders, in individuals without a personal or family history. It is only relevant to partners of affected individuals or partners of carriers detected through targeted testing due to family history.

In most autosomal recessive conditions, cascade testing of wider family members and unrelated partners is NOT indicated. Clinicians wishing to request a test under this indication should check with their GLH whether the test is feasible prior to offering testing to patients.

Testing is not usually indicated in this context because the test results have a minimal impact on the risk of health problems in pregnancies beyond the parents and siblings of the affected individual:

1. For most genes, interpreting the results of population risk carrier testing is complex, and the proportion of detected variants which can be confidently used for reproductive purposes is low
2. Carrier testing at population risk is not able to rule out an unrelated partner being a carrier of the condition, only reduce the likelihood
3. The carrier frequency of most autosomal recessive conditions is low, such that the marginal gain from genetic testing of an unrelated partner has limited impact on the prenatal decision-making process

However, there are circumstances in which the chance of a baby being affected is more substantial, and/or there are early detection/screening strategies available to biallelic offspring and carrier testing is feasible. Testing is more likely to be considered appropriate where the following criteria are met:

1. Presence of a homozygous or compound heterozygous genotype in a baby would have a sufficiently predictable effect to permit reproductive choices to be made; for example, carrier testing for haemochromatosis or alpha-1-antitrypsin deficiency is NOT appropriate as it is not possible to predict from the genotype whether an affected baby will ever develop medical problems
2. The associated gene is well-understood and does not contain a high level of novel, benign variation, such that it is likely to be possible to interpret variants found on full gene testing in individuals at population risk; in this context only likely pathogenic or pathogenic variants according to the ACGS / ACMG classification will be reported
3. Presence of a biallelic genotype in the couple's offspring would result inform/determine clinical management e.g. early detection and/or prevention strategies.

PLUS one of the following:

1. The carrier frequency of the condition is higher than 1 in 70 (in the relevant population(s) for the patient to be tested)
2. The couple are consanguineous (second cousins or closer); where this is the only criterion that is met, testing will be limited to the known familial variant.

R246已知携带者伴侣的人群风险携带者检测 全国共识常染色体隐性疾病

检测标准

本临床指征涉及对患有常染色体隐性遗传病或已知为携带者且有家族史的个体的伴侣进行携带者检测，条件为：

- 当前或未来妊娠的管理将受到检测结果影响，且该夫妇符合 PGD 或临床指征 R448 产前检测下的产前诊断资格

或

- 对伴侣进行携带者检测可行，并将为其子女的临床管理(包括监测)提供信息/决定临床管理。

本临床指征不旨在影响与无个人或家族史的个体中常染色体隐性遗传病相关基因的偶然携带者发现报告相关的决策。它仅适用于患者的伴侣或通过因家族史而进行的靶向检测发现的携带者的伴侣。

在大多数常染色体隐性遗传病中，不建议对更广泛家庭成员和无血缘关系伴侣进行级联检测。希望根据本指征申请检测的临床医生应在向患者提供检测前与其 GLH 核实检测是否可行。

在此背景下通常不建议进行检测，因为检测结果对患者父母和兄弟姐妹之外的妊娠健康问题风险影响极小：

1. 对于大多数基因，解读人群风险携带者检测的结果较为复杂，且可自信用于生育目的所检出变异的比例较低

2. 人群风险携带者检测无法排除无血缘关系伴侣为该病携带者，只能降低可能性

3. 大多数常染色体隐性遗传病的携带者频率较低，因此对无血缘关系伴侣进行基因检测的边际收益对产前决策过程影响有限

然而，在某些情况下，婴儿患病的几率更高，和/或存在可用于双等位基因后代的早期发现/筛查策略，且携带者检测可行。在满足以下标准时，检测更可能被认为适当：

1. 婴儿存在纯合或复合杂合基因型将具有足够可预测的影响，从而允许做出生育选择；例如，血色病或α-1-抗胰蛋白酶缺乏症的携带者检测不适当，因为无法从基因型预测患病婴儿是否会发展出医学问题

2. 相关基因已被充分了解，且不包含大量新的良性变异，因此对人群风险个体进行全基因检测所发现的变异很可能可以解读；在此背景下，仅报告根据 ACGS / ACMG 分类的致病变异或可能致病变异

3. 夫妇后代存在双等位基因型将为其临床管理提供信息/决定临床管理，例如早期发现和/或预防策略。

PLUS以下之一：

1. 该疾病的携带者频率高于 1/70(在受检患者的相关人群中)

2. 夫妇为近亲婚配(二级表亲或更近)；若这是唯一满足的标准，检测将限于已知家族变异。

In exceptional circumstances and after discussion with the home GLH, testing may be considered appropriate in situations where the gene is suitable for testing and there are known pathogenic variant(s), that can be tested for, that account for the majority of cases in the relevant population(s) for the patient to be tested; in this context, the test will primarily target the pathogenic variants that account for the majority of cases in the relevant population(s).

NOTE: The following specific clinical indications should be used instead for the relevant disorders:

- R181 Congenital adrenal hyperplasia carrier testing
- R361 Sickle cell, thalassaemia and other haemoglobinopathies trait or carrier testing
- R252 SMA carrier testing at population risk for partners of known carriers
- R185 Cystic fibrosis carrier testing

Table 1. Example autosomal recessive conditions with a carrier frequency higher than 1 in 70 in these example populations, which would be covered by this clinical indication. Note these are examples only and the indication covers a much wider range of conditions and populations where evidence of high carrier frequency is available and the criteria above are met.

Disease	Gene	Carrier frequency
Deafness, autosomal recessive 1A	*GJB2*	1 in 50 in European populations
Gaucher disease	*GBA*	1 in 25 in Ashkenazi population
Phenylketonuria	*PAH*	1 in 50 in European populations
Tay-Sachs disease	*HEXA*	1 in 30 in Ashkenazi population

Where in Pathway

As dictated by clinical situation

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Core or Specialised; depending on the autosomal disorder being investigated

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R246.1	Specific target Single gene sequencing	Singleton	Small variants	Single gene(s)	Relevant single gene	Single gene sequencing >=10 amplicons

在特殊情况下，且与所在 GLH 讨论后，若基因适合检测且存在已知致病变异可供检测，这些变异解释了受检患者相关人群中的大多数病例，则检测可能被认为适当；在此背景下，检测将主要针对解释相关人群中大多数病例的致病变异。

注意：对于相关疾病，应改用以下特定临床指征：

- R181 先天性肾上腺皮质增生症携带者检测
- R361 镰状细胞病、地中海贫血及其他血红蛋白病特质或携带者检测
- R252 已知携带者伴侣的群体风险 SMA 携带者检测
- R185 囊性纤维化携带者检测

表1. 在这些示例人群中携带者频率高于 1/70 的常染色体隐性遗传病示例，本临床指征将涵盖这些疾病。注意这些仅为示例，该指征涵盖更广泛的疾病和人群，只要有高携带者频率的证据且满足上述标准。

疾病	基因	携带者频率
耳聋，常染色体隐性1A	*GJB2*	欧洲人群中50分之一
戈谢病	*GBA*	阿什肯纳兹人群中每25人中有1人
苯丙酮尿症	*PAH*	欧洲人群中50分之一
泰-萨克斯病	*HEXA*	阿什肯纳兹人群中每30人中有1人

通路中的位置

视临床情况而定

申请专科

- 临床遗传学

专科服务组

- 核心或专科；取决于所调查的常染色体疾病

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R246.1	特定靶标 单基因 测序	单人	小变异	单基因	相关单基因	单基因 测序 >=10 扩增子

R321 Maternal cell contamination testing

Testing Criteria

Pregnancy requiring maternal cell contamination to inform interpretation of other testing, for example invasive prenatal testing, tests on fetal tissues or tests performed on cord blood

Testing will often be initiated by the testing laboratory but relevant samples will be required in advance of testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

As appropriate

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R321.1	Genomewide Identity testing	Multiple affected individuals	Identity	Genomewide	Genomewide	Identity testing

R321母源细胞污染检测

检测标准

妊娠需要进行母源细胞污染检测以辅助其他检测的解读，例如侵入性产前检测、胎儿组织检测或脐带血检测

检测通常由检测实验室发起，但需要在检测前提前提供相关样本

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

酌情

申请专科

• 临床遗传学

• 基因组实验室

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R321.1	全基因组范围身份鉴定	多个受累个体	身份	全基因组范围	全基因组范围	身份鉴定检测

R320 Invasive prenatal diagnosis requiring fetal sexing

Testing Criteria

Pregnancy requiring sexing on invasive prenatal sample to inform management

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

As appropriate

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R320.1	Sex determination testing	Singleton	Aneuploidy	Genomewide	Other	Common aneuploidy testing

R320需要胎儿性别鉴定的侵入性产前

检测标准

妊娠需通过对侵入性产前样本进行性别鉴定以指导管理

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

酌情

申请专科

• 临床遗传学

• 基因组实验室

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R320.1	性别鉴定检测	单人	非整倍体	全基因组范围	其他	常见非整倍体检测

R263 Confirmation of uniparental disomy

Testing Criteria

Confirmation of probable UPD identified by methylation testing at imprinted loci and UPD identified via other routes, for example SNP array, exome or genome sequencing. This could include testing for mosaic genome-wide UPD

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

As appropriate

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R263.1	Specific target UPD testing	Trio	Small variants	Single interval	As relevant to clinical setting	UPD testing

R263确认单亲二体

检测标准

确认通过印记位点甲基化检测发现的可能UPD，以及通过其他途径(例如SNP微阵列、外显子组或基因组测序)发现的UPD。这可能包括针对嵌合型全基因组UPD的检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

酌情

申请专科

• 临床遗传学

• 基因组实验室

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R263.1	特定靶标UPD检测	三人组	小变异	单一区间	根据临床情况而定	UPD检测

R264 Identity testing

Testing Criteria

Where biological relationships need to be determined to guide diagnostic interpretation or alter advice

Where in Pathway

N/A

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R264.1	Identity testing	Singleton	Identity	Other	Other	Identity testing

R264身份检测

检测标准

当需要确定生物学关系以指导诊断解读或改变建议时

通路中的位置

不适
用

申请专科

• 临床遗传学
• 基因组实验室

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R264.1	身份鉴定检测	单人	身份	其他	其他	身份鉴定检测

400 20th May 2026 v9.1

R111 X-inactivation testing

Testing Criteria

Clinical setting where X-inactivation testing will alter clinical management and/or assist reclassification of variant using the ACGS / ACMG guidelines

Where in Pathway

After MDT discussion

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R111.1	X-inactivation testing	Singleton	Methylation	Single interval	Other	X-inactivation testing

R111X染色体失活检测

检测标准

X 染色体失活检测将改变临床管理及/或协助依据 ACGS / ACMG 指南对变异进行重新分类的临床情境

通路中的位置

经MDT讨论后

申请专科

• 临床遗传学

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R111.1	X染色体失活检测	单人	甲基化	单一区间	其他	X染色体失活检测

R370 Validation of unaccredited findings

Testing Criteria

Validation of the presence, and clinical interpretation, of a genomic variant detected outside of an accredited process (e.g. from research findings), when required for diagnostic reporting.

Examples of settings in which this indication may be used include:

- Variants detected outside of an accredited process where the accuracy of the result needs to be validated.
- where the sample has passed outside an accredited pipeline and confirmation of sample identity is required

Where in Pathway

Following primary test where required

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R370.1	Specific target Targeted variant testing	Singleton	Small variants	Single interval	Specific Target	Targeted variant testing

R370未获认可结果的验证

检测标准

对在获认可流程之外检测到的基因组变异的存在性及临床解读进行验证，且为诊断报告所需时。可使用该指征的情境示例包括：

- 在获认可流程之外检测到的变异，其结果准确性需要已验证。
- 样本已脱离获认可流程，且需要确认样本身份时

通路中的位置

在需要时进行后续主要检测

申请专科

- 临床遗传学
- 基因组实验室

专科服务组

- 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R370.1	特定靶标靶向变异检测	单人	小变异	单一区间	特定靶标	靶向变异检测

R443 Confirmation test

Testing Criteria

Confirmation of the presence/absence of a genomic finding identified through primary testing/analysis, where additional testing using a second technique is required to report the primary test result. This test code is for use by genomic laboratories only and not orderable by clinicians.

Clinical request to confirm the presence of a variant identified outside of an NHS diagnostic laboratory should use R370.

Requests to confirm germline origin of variants detected through somatic testing should use R240.

Examples of where this test is to be used include; where MLPA is required in addition to NGS in cases where copy number variant analysis only has not achieved the required quality threshold, or where orthogonal STR testing is required based on WGS analysis results. It is anticipated that in the majority of cases this confirmation test result will form part of the primary test report and not reported separately.

Where in Pathway

Following primary test where required

Requesting Specialties

- Genomics laboratory

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R443.1	Specific target Targeted variant testing	Singleton	Small variants, CNVs and STRs	Single interval	Specific Target	Targeted variant testing

R443确认检测

检测标准

确认通过初次检测/分析发现的基因组结果的存在/缺失，且需要使用第二种技术进行额外检测以报告初次检测结果。该检测代码仅供基因组实验室使用，临床医生不可开具。

临床申请确认在 NHS 诊断实验室之外检测到的变异的存在性
应使用 R370。

要求确认通过体细胞检测发现的变异的胚系来源的申请应使用 R240。

使用该检测的情境示例包括：当拷贝数变异分析单独未能达到所需质量阈值时，除 NGS 外还需要 MLPA 的情况，或基于 WGS 分析结果需要正交短串联重复序列检测的情况。预计在大多数情况下，该确认检测结果将构成初次检测报告的一部分，而不单独报告。

通路中的位置

在需要时进行后续主要检测

申请专科

• 基因组实验室

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R443.1	特定靶标靶向变异检测	单人	小变异，CNVs和短串联重复序列	单一区间	特定靶标	靶向变异检测

R442 Variant Re-interpretation

Testing Criteria

Interpretation of a known variant to determine if the pathogenic status has changed since primary analysis and reporting or a previous re-interpretation. Re-interpretation of a variant may be performed as a result of;

- A request from a clinician responsible for a patient with a reported variant of uncertain significance,

OR

- new evidence available that will likely change the classification of a variant. For example, the identification of additional patient(s) with the same genetic variant or new functional evidence,

AND

- where either; there is new clinical information related to the patient or their family, or sufficient time has passed that there may be additional published evidence or knowledge, that could result in a change to the classification of the variant.

Where in Pathway

Following primary test where required

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R442.1	Specific target Targeted variant testing	Singleton	Small variants	Single interval	Specific Target	Targeted variant testing

R442变异重新解读

检测标准

对已知变异进行解读，以确定自初次分析和报告或既往重新解读以来其致病状态是否发生变化。变异的重新解读可因以下原因进行：

- 负责携带已报告意义未明变异患者的临床医生提出申请，

或

- 有新证据可用且可能改变变异的分类。例如，发现携带相同遗传变异的额外患者或新的功能证据，

和

- 存在以下任一情况：有与患者或其家族相关的新临床信息，或已过去足够时间以致可能有额外的已发表证据或知识，从而可能导致变异分类发生变化。

通路中的位置

在需要时进行后续主要检测

申请专科

- 临床遗传学
- 基因组实验室

专科服务组

- 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R442.1	特定靶标靶向变异检测	单人	小变异	单一区间	特定靶标	靶向变异检测

R375 Family follow-up testing to aid variant interpretation

Testing Criteria

Family follow-up testing to aid variant interpretation

Where in Pathway

Where requested by the laboratory

Requesting Specialties

- Clinical Genetics
- Other

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R375.1	Specific target Targeted variant testing	Singleton	Small variants	Single interval	Specific Target	Targeted variant testing

R375家族随访检测以协助变异解读

检测标准

家族随访检测以辅助变异解读

通路中的位置

应实验室要求

申请专科

• 临床遗传学

• 其他

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R375.1	特定靶标靶向变异检测	单人	小变异	单一区间	特定靶标	靶向变异检测

R387 Reanalysis of existing data

Testing Criteria

Reanalysis of data which has previously been interpreted and reported is required, due to:

1. New clinical information or clinical events which would substantially change the relevant genomic target, OR
2. Sufficient time has passed since the initial analysis that new gene discovery will have substantially increased the relevant genomic target, OR
3. A technical or scientific advance requires reanalysis of a group of tests to detect an important new source of actionable diagnoses

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following discussion with the genomics laboratory to ensure stored data is suitable for reanalysis and that the request is aligned to the national guidance for reanalysis (https://future.nhs.uk/NHSgenomics/view?objectId=154355365).

The R387 request form should be used to provide all required information. This can be obtained from the Genomic Laboratory Hub or via NHS Futures for those with access (https://future.nhs.uk/NHSgenomics/view?objectId=156197061).

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R387.1	Reanalysis of existing data	Multiple affected individuals	Other	Other	As per updated indication	Other

R387现有数据的重新分析

检测标准

因以下原因需要对既往已解读和报告的数据进行重新分析：

1. 新的临床信息或临床事件将实质性改变相关基因组靶标，或
2. 自初次分析以来已过去足够时间，以致新基因发现将实质性扩大相关基因组靶标，或
3. 技术或科学进步要求对一组检测进行重新分析，以发现重要的可干预诊断新来源

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

在与基因组实验室讨论后，以确保存储数据适合重新分析且申请符合国家重新分析指南(https://future.nhs.uk/NHSgenomics/view?objectId=154355365)。应使用 R387 申请表提供所有所需信息。可从基因组实验室中心获取，或通过 NHS Futures 供有访问权限者获取(https://future.nhs.objectId=156197061)。

申请专科

• 临床遗传学
• 基因组实验室

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R387.1	重新分析现有数据	多个受累个体	其他	其他	根据更新后的适应症	其他

R296 RNA analysis of variants

Testing Criteria

Variant(s) requiring RNA analysis to aid interpretation where a molecular diagnosis will guide management or alter advice through reclassification of a variant from ACGS / ACMG variant of uncertain significance to likely pathogenic or pathogenic.

Testing should be discussed in advance with the laboratory

Where in Pathway

Following MDT discussion of candidate splice variant

Requesting Specialties

- Clinical Genetics
- Genomics laboratory

Specialist Service Group

- Core or Specialised; depending on the disorder and associated variant being investigated
-

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R296.1	Specific target RNA analysis	Singleton	Complex variants	Other	As dictated by variant under investigation	Other

R296变异的RNA分析

检测标准

需要 RNA 分析以协助解读的变异，且分子诊断将指导管理或通过将变异从 ACGS / ACMG 意义未明变异重新分类为可能致病或致病来改变建议。

检测应事先与实验室讨论

通路中的位置

经MDT讨论候选剪接变异后

申请专科

• 临床遗传学

• 基因组实验室

专科服务组

• 核心或专科；取决于所调查的疾病及相关变异

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R296.1	特定目标RNA分析	单人	复合体变异	其他	根据所分析的变异而定调查	其他

R346 DNA to be stored

Testing Criteria

To be requested where genetic testing is likely to be required in future, but further information or discussion is needed before a test request is made

Where in Pathway

At any time, including where a sample is available e.g. because phlebotomy is being undertaken for other investigations and a future genetic test is likely to be required

Requesting Specialties

- Clinical Genetics
- Other

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R346.1	DNA Storage	Singleton	Other	Other	No target identified at this stage	Other

R346DNA予以储存

检测标准

在未来可能需要遗传检测，但在提出检测申请前需要进一步信息或讨论时申请

通路中的位置

任何时候，包括有样本可用时，例如因其他检查正在进行采血且未来可能需要遗传检测

申请专科

• 临床遗传学

• 其他

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R346.1	DNA存储	单人	其他	其他	此阶段未确定目标	其他

R373 RNA to be stored

Testing Criteria

To be requested where RNA testing is likely to be required in future, but further information or discussion is needed before a test request is made

Where in Pathway

Following discussion with the laboratory

Requesting Specialties

- Clinical Genetics
- Other

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R373.1	RNA Storage	Singleton	Other	Other	No target identified at this stage	Other

R373RNA予以储存

检测标准

在未来可能需要 RNA 检测，但在提出检测申请前需要进一步信息或讨论时申请

通路中的位置

与实验室讨论后

申请专科

• 临床遗传学

• 其他

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R373.1	RNA储存	单人	其他	其他	此阶段未确定目标	其他

R322 Skin fibroblasts to be cultured and stored

Testing Criteria

Skin fibroblast sample requiring culture and storage for potential future testing

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

As appropriate

Requesting Specialties

- Clinical Genetics
- Dermatology
- Metabolic Medicine
- Neurology
- Other

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R322.1	Skin fibroblast culture and storage	Singleton	Other	Other	No target identified at this stage	Other

R322皮肤成纤维细胞进行培养并储存

检测标准

需要培养和储存皮肤成纤维细胞样本以备将来可能进行的检测

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

酌情

申请专科

- 临床遗传学
- 皮肤病学
- 代谢医学
- 神经科
- 其他

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R322.1	皮肤成纤维细胞培养与保存	单人	其他	其他	此阶段未确定目标	其他

R374 Other sample to be stored

Testing Criteria

To be requested where testing of other sample types (for example, lymphocyte culture) is likely to be required in future, but further information or discussion is needed before a test request is made

Overlapping indications

- R346 DNA to be stored, R373 RNA to be stored and R322 Skin fibroblasts to be cultured and stored should be used instead where relevant

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

Following discussion with the laboratory

Requesting Specialties

- Clinical Genetics
- Other

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R374.1	Other sample storage	Singleton	Other	Other	No target identified at this stage	Other

R374其他样本进行储存

检测标准

在将来可能需要对其他样本类型(例如淋巴细胞培养)进行检测，但在提出检测申请之前需要进一步的信息或讨论时申请

重叠指征

- R346 DNA 待储存，R373 RNA 待储存，R322 皮肤成纤维细胞待培养和储存
  应在相关情况下改用

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

与实验室讨论后

申请专科

- 临床遗传学
- 其他

专科服务组

- 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R374.1	其他样本储存	单人	其他	其他	此阶段未确定目标	其他

R428 Patient receiving solid organ transplantation (only in cases where passenger lymphocyte syndrome is suspected)

Testing Criteria

Patient is post-solid organ transplant and the treating clinician has concerns they have developed passenger lymphocyte syndrome based on their clinical presentation; i.e. they have developed cytopenias not wholly explainable via other causes.

Allogeneic transplant where chimerism knowledge will aid patient management.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Overlapping indications

- M242 Any patient receiving solid organ transplantation – same test duplicated in the cancer Test Directory

Where in Pathway

As dictated by clinical situation

Requesting Specialties

- Oncology
- Appropriate specialist referring clinician

Specialist Service Group

- Core

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R428.1	Patient undergoing allogeneic solid organ transplantation STR testing	Singleton	Short tandem repeats	Targeted variant testing	Relevant gene(s) or loci	STR testing
R428.2	Patient undergoing allogeneic solid organ transplantation CNV testing	Singleton	CNVs	Targeted variant testing	Sex chromosomes	FISH

R428接受实体器官移植的患者(仅在怀疑过客淋巴细胞综合征的情况下)

检测标准

患者为实体器官移植后，且主治临床医生根据其临床表现担心患者已发展为过客淋巴细胞综合征；即患者已出现不能完全用其他原因解释的血细胞减少

异基因移植中嵌合体知识有助于患者管理的情况。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

重叠指征

• M242 任何接受实体器官移植的患者--同一检测在肿瘤检测目录中重复列出目录

通路中的位置

视临床情况而定

申请专科

• 肿瘤学

• 适当的专科转诊临床医生

专科服务组

• 核心

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R428.1	正在接受异基因实体器官移植 STR检测	单人	短串联重复	靶向变异检测	相关基因或基因座	STR检测
R428.2	正在接受异基因实体器官移植 CNV检测	单人	拷贝数变异	靶向变异检测	性染色体	FISH

R409 Linkage testing for recognisable Mendelian disorders

Testing Criteria

Patients with a recognisable mendelian disorder where linkage testing will guide patient management (if informative),.

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Where in Pathway

As dictated by clinical situation

Requesting Specialties

- Clinical Genetics
- Other

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R409.1	Linkage testing for other recognisable Mendelian disorders	Multiple affected individuals	Other	Single gene(s) or loci	Relevant gene(s) or loci	Linkage analysis

R409连锁分析用于可识别的孟德尔疾病

检测标准

患有可识别的孟德尔疾病且连锁分析将指导患者管理(如信息充分)的患者。

检测转诊将由基因组实验室进行分诊；检测应针对遗传或基因组诊断将指导先证者或家庭管理的患者。

通路中的位置

视临床情况而定

申请专科

• 临床遗传学

• 其他

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R409.1	连锁检测用于其他可识别的孟德尔疾病	多个受累个体	其他	单基因或基因座	相关基因或基因座	连锁分析

R447 Validation of WGS Diagnostic discovery findings

Testing Criteria

Analytical validation and/or confirmation of putative diagnostic findings returned from whole genome sequencing data from 100,000 genome project or GMS patients, through the NHS Diagnostic discovery pathways.

This will involve analytical validation and interpretation of the genomic variant(s) with or without confirmatory testing by an orthogonal test as required.

Overlapping indications

R370 validation testing should be used for the validation of potential diagnostic findings identified outside of the WGS Diagnostic Discovery pathway.

Where in Pathway

Following primary test where required

Requesting Specialties

- Genomics laboratory

Specialist Service Group

- Core or Specialised; depending on the clinical scenario

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R447.1	Validation of WGS Diagnostic discovery findings	Singleton	Small variants, CNVs, STRs	Single interval	Specific Target	Targeted variant testing

R447WGS诊断发现的验证

检测标准

通过 NHS 诊断发现途径，对来自 100,000 基因组计划或 GMS 患者的全基因组测序数据所返回的推定诊断发现进行分析验证和/或确认
通路。

这将涉及对基因组变异进行分析验证和解读，并根据需要进行或不进行正交检测的确认检测。

重叠指征

R370 验证检测应用于验证在 WGS 诊断发现途径之外识别的潜在诊断发现。

通路中的位置

在需要时进行后续主要检测

申请专科

• 基因组实验室

专科服务组

• 核心或专科；取决于临床情况

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R447.1	WGS验证 诊断性 发现性结果	单人	小变异， CNVs、STRs	单一区间	特定靶标	靶向 变异检测

R448 Prenatal testing

Testing Criteria

Ongoing pregnancy requiring prenatal testing for a specific disorder where the familial variant(s) have already been identified in a relative

Where in Pathway

As dictated by clinical situation

Requesting Specialties

Clinical Genetics

Specialist Service Group

- Core or Specialised; depending on the clinical scenario.

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R448.1	Prenatal testing	Singleton	Small variants, CNVs, STRs	Single interval	Specific Target	Targeted variant testing

R448产前检测

检测标准

正在进行的妊娠需要对特定疾病进行产前检测，且家族性变异已在亲属中识别

通路中的位置

视临床情况而定

申请专科

临床遗传学

专科服务组

• 核心或专科；取决于临床情况。

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R448.1	产前检测	单人	小变异，CNVs、STRs	单一区间	特定靶标	靶向变异检测

R431 Genome-wide DNA Methylation Profiling to Aid Variant Interpretation

Testing Criteria

Patients must have a plausibly significant variant of uncertain significance in a gene which is covered by this test (see below).

The list of disorders/genes is available at: https://mft.nhs.uk/app/uploads/2023/08/Methylation-Array-Panel-content-for-EpiSign.pdf.

Patients can be referred by clinical genetics or from an appropriate specialty via consultation with clinical genetics.

Please note that this test requires DNA extracted from peripheral blood preferably obtained at more than 6 months of age.

Where in Pathway

Following discussion with Clinical Genetics and the testing laboratory

Requesting Specialties

- Clinical Genetics

Specialist Service Group

- Multi specialty

Associated Tests

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R431.1	Genome-wide DNA Methylation Profiling to Aid Variant Interpretation	Singleton	Methylation signature	Genomewide	Genomewide	Methylation microarray

R431全基因组DNA甲基化分析以辅助变异解读

检测标准

患者必须在本检测所覆盖的基因中(见下文)存在可能具有显著意义的意义未明变异。

疾病/基因列表可在以下网址获取：https://mft.nhs.uk/app/uploads/2023/08/Methylation-Array-Panel-EpiSign 检测内容.pdf

患者可由临床遗传学转诊，或由相应专科在与临床遗传学协商后转诊。

请注意，本检测需要从外周血提取的DNA，最好在6月龄以上时采集。

通路中的位置

与临床遗传学部门及检测实验室讨论后

申请专科

- 临床遗传学

专科服务组

- 多专科

相关检测

代码	名称	最佳家庭结构	范围	目标类型	目标名称	方法
R431.1 全基因组DNA	甲基化谱分析辅助变异解读	单人	甲基化特征	全基因组范围	全基因组范围	甲基化微阵列（基因芯片）

Change Log for April and May 2026 updates

Date	Document Name	Version	Summary of Changes
May 2026	Rare and Inherited Disease eligibility criteria May 2026	May 2026 v9.1	R438 Paediatric pseudo-obstruction syndrome Moved the note about Hirschsprung disease from “Where in the Pathway” to “Testing Criteria”
May 2026	Rare and Inherited Disease eligibility criteria May 2026	May 2026 v9.1	R453 Monogenic short stature SHOX gene has remained on this panel and therefore the note in the overlapping Clinical Indication for SHOX deficiency stating that this test should be ordered if SHOX deficiency is suspected as SHOX is not included as a target on R453 panel, has been removed.
May 2026	Rare and Inherited Disease eligibility criteria May 2026	May 2026 v9.1	Formatting correction: removed track changes that were on the final document in error under the following CIs: R47, R78, R82 and R381.
May 2026	Rare and Inherited Disease eligibility criteria May 2026	May 2026 v9.1	R32 Retinal disorders Added a note in the Testing Criteria to state that for retinal hamartoma, other more appropriate Clinical Indications should be used where the patient meets the eligibility criteria, for example, R221 Familial tumours of the nervous system (as NF2 is not included on the retinal disorders panel) or R228 Tuberous sclerosis (as TSC1 & TSC2 are not included on the retinal disorders panel).
May 2026	Rare and Inherited Disease eligibility criteria May 2026	May 2026 v9.1	R457 Sarcoma of possible germline origin In error had missed off an additional criterion for chordoma: Multiple benign notochordal tumour / ecchordosis physaliphora. Tidied criteria so that “where other germline panel or paired WGS has not been undertaken” is now placed upfront rather than in every criterion point.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R137 Congenital heart disease – microarray Additional eligibility and amendments made to the criteria.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R125 Thoracic aortic aneurysm or dissection Removal of criterion 3., 4. And 7.. Change in z score threshold in children from >2 to >3
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R132 Dilated and arrhythmogenic cardiomyopathy Error correction: removal of 1c
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R135 Paediatric or syndromic cardiomyopathy Removal of “a second condition” in criterion 2.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R140 Elastin-related phenotypes In overlapping CIs, specifying that patients must meet the criteria for the overlapping CIs if these tests are ordered instead.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R441 Unexplained death in infancy and sudden unexplained death in childhood Changes to the eligibility criteria to include Joint Agency Response review and DNA requirements from biological parents.

变更日志用于2026年4月和5月更新

日期	文档名称	版本	变更摘要
2026年5月	罕见病与遗传病 检测资格标准 2026年5月	2026年5月 v9.1	R438 儿童假性肠梗阻综合征 将关于Hirschsprung病的说明从“通路中的位置”移至“检测标准”
2026年5月	罕见病与遗传病 检测资格标准 2026年5月	2026年5月 v9.1	R453 单基因性矮小症 SHOX基因仍保留在本 panel 中，因此重叠临床 指征中关于SHOX缺陷的说明--即若怀疑SHOX缺陷应申请本检测，因为SHOX未作为靶标纳入R453 panel--已被删除。
2026年5月	罕见病与遗传病 检测资格标准 2026年5月	2026年5月 v9.1	格式更正：删除了修订痕迹，其 在以下临床指征下错误地留在了最终文件中： R47、R78、R82和R381。
2026年5月	罕见病与遗传病 检测资格标准 2026年5月	2026年5月 v9.1	R32 视网膜疾病 在检测标准中增加说明：对于视网膜错构瘤，若患者符合检测资格标准，应使用其他更合适的临床指征，例如R221神经系统家族性肿瘤(因为NF2未纳入视网膜疾病 panel)或R228结节性硬化症(因为TSC1和TSC2未纳入视网膜疾病 panel)。
2026年5月	罕见病与遗传病 检测资格标准 2026年5月	2026年5月 v9.1	R457 可能源于生殖系的肉瘤 错误地遗漏了脊索瘤的一项附加标准：多发性良性脊索肿瘤/颅内脊索瘤。 整理了标准，使“未进行其他胚系 panel 或配对WGS”现置于前面，而非每个标准条目中。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R137 先天性心脏病 – 微阵列（基因芯片） 对以下内容所作的附加资格条件与修订标准。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R125 胸主动脉瘤或夹层 删除标准3、4和7。儿童z评分阈值从>2改为>3
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R132 扩张型与致心律失常性心肌病 纠错：删除1c
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R135 儿童期或综合征性心肌病 删除标准2中的“第二病症”。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R140 弹性蛋白相关表型 在重叠临床指征中，明确若改为申请这些检测，患者必须符合重叠临床指征的标准。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R441 婴儿期不明原因死亡与猝死 儿童期不明原因死亡 检测资格标准的变更，纳入联合机构响应审查以及对生物学父母的DNA要求。

Date	Document Name	Version	Summary of Changes
			Addition of exclusion criteria Amendment to “where in the pathway”. Requesting specialties updated to state that this is in liaison with the designated doctor for child deaths.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R26 Likely common aneuploidy Removed R297 from the overlapping Clinical Indications as R297 has been retired – see separate entry for R297 for details.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R27 Paediatric disorders Addition of criteria for unexplained epilepsy due to retirement of separate CI for epilepsy (R59) Additional statement included for R14 in overlapping CIs Addition of psychiatry as a requesting specialty
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R29 Intellectual disability Retirement of CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R377 Intellectual disability – microarray only Retirement of CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R47 Angelman syndrome Retirement of R47.2 as MLPA analysis can be done as part of R47.1 methylation testing. Addition to scope for R47.1 to include CNVs.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R48 Prader-Willi syndrome Addition of clinical features to the eligibility criteria to support appropriate referrals. Where in the pathway updated so that there is no longer a need for consultant clinical geneticist to assess prior to request for testing. Retirement of R48.2 as MLPA analysis can be done as part of R48.1 methylation testing. Addition to scope for R48.1 to include CNVs.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R69 Hypotonic infant Addition of R452 Silver Russel Syndrome / Temple syndrome to overlapping CIs. Removal of confirmatory STR CITT R69.6 as the generic code for confirmation test should be used instead.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R314 Ambiguous genitalia presenting neonatally Change of CI name to ambiguous genitalia. Removing restriction to present neonatally. Amended criteria. Tag line added to state that not all associated tests will be undertaken in every case – the reason for referral will indicate what tests will be required.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R142 Glucokinase-related fasting hyperglycaemia Added specialist midwifery to the requesting specialties.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R146 Differences in sex development

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			增加排除标准 对“路径中的位置”的修订。 申请科室更新为说明此检测与儿童死亡指定医生协商进行。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R26 可能为常见非整倍体 从重叠的临床检测中移除了 R297 适应症：R297 已废止--详情见 R297 的单独条目。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R27 儿童期疾病 因癫痫的独立临床指征(R59)已废止，增加不明原因癫痫的 针对重叠部分中的 R14 增加了附加说明 检测资格标准 增加精神科作为申请专科
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R29 智力障碍 检测资格标准的废止
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R377 智力障碍 - 仅微阵列 检测资格标准的废止
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R47 Angelman综合征 R47.2废止，因为MLPA分析可作为R47.1甲基化检测的一部分进行。R47.1的范围增加以纳入CNV。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R48 Prader-Willi综合征 在检测资格标准中增加临床特征，以支持适当的转诊。 更新通路中的位置，使申请检测前不再需要顾问临床遗传学家进行评估。 R48.2废止，因为MLPA分析可作为R48.1甲基化检测的一部分进行。R48.1的范围增加以纳入CNV。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R69 肌张力低下婴儿 将R452 Silver Russel综合征/Temple综合征添加至重叠CI。 删除确认性STR CITT R69.6，因为应使用确认检测的通用 改为。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R314 新生儿期表现出的外生殖器性别不明 临床指征名称变更为外生殖器模糊。取消仅限于新生儿期表现的限制。修订了标准。 增加标签行，说明并非每例都会进行所有相关检测--转诊原因将表明需要哪些检测。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R142 葡萄糖激酶相关空腹高血糖 增加了专科助产士到申请中 专科。
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R146 性发育差异

Date	Document Name	Version	Summary of Changes
			Removed R297 as an overlapping clinical indication as R297 has been retired (see separate entry) and added R468 Possible sex chromosome aneuploidy or structural rearrangement – Targeted Chromosome Analysis, as new overlapping CI.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R452 Silver Russell Syndrome and Temple Syndrome Clinical features for Temple Syndrome added to the eligibility criteria.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R453 Monogenic short stature Included table from the BSPED for normal short screen primary investigations recommend in children referred to secondary or tertiary care with short stature. Added to overlapping CI R52 Short stature – SHOX deficiency that this test should be ordered if SHOX deficiency is suspected as SHOX is not included as a target on the R453 panel.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R49 Beckwith-Wiedemann syndrome Retired R49.2 as CNVs are included on the methylation test under R49.1. Scope for R49.1 expanded to include CNVs.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R50 Isolated hemihypertrophy or macroglossia Retired R50.2 as CNVs are included on the methylation test under R50.1. Scope for R50.1 expanded to include CNVs.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R267 Temple syndrome – maternal uniparental disomy 14 Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R180 Congenital adrenal hyperplasia diagnostic test Added to the criteria: Female adult with raised 17-OHP and at least one of the following: hirsutism, frontal baldness, delayed menarche or infertility
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R181 Congenital adrenal hyperplasia carrier testing Changed from targeted variant testing to single gene sequencing
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R388 Linkage testing for congenital adrenal hyperplasia Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R154 Hypophosphataemia or rickets Addition to eligibility criteria where ALP is low.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R223 Inherited phaeochromocytoma and paraganglioma excluding NF1 Removal from criterion 6. renal cell cancer (any age)
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R158 Lipodystrophy – childhood onset Changed CI name to Severe insulin resistance and lipodystrophy syndromes. Removed need for childhood onset in the eligibility criteria. Included severe insulin resistance in the criteria.

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			删除R297作为重叠临床指征，因为R297已废止(见单独条目)，并增加R468可能的性染色体非整倍体或结构重排--靶向 染色体分析，作为新的重叠CI。
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R452	R452 Silver Russell综合征与Temple综合征 Temple 综合征的临床特征已添加到资格标准中。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R453	R453 单基因矮身材 纳入BSPED的表格，用于因矮小转诊至二级或三级医疗的儿童所推荐的正常矮小筛查初步检查 身材。 在重叠临床指征R52矮身材--SHOX缺陷中增加说明：若怀疑SHOX缺陷应申请本检测，因为SHOX未作为靶标纳入R453 panel。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R49	R49 Beckwith-Wiedemann综合征 停用 R49.2，因为 CNV 已纳入 R49.1 下的甲基化检测。R49.1 的范围扩大至包含 CNV。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R50	R50 孤立性偏身肥大或巨舌症 停用 R50.2，因为 CNV 已纳入 R50.1 下的甲基化检测。R50.1 的范围扩大至包含 CNV。
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R267	Temple综合征--母源单亲二体14号染色体二体 已退役 CI
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R180	R180 先天性肾上腺增生症诊断检测 标准中新增：17-OHP 升高的成年女性，且至少具备以下一项：多毛症、额部秃发、月经初潮延迟或不孕
2026年4月 罕见与遗传性	疾病检测资格标准 2026年4月	2026年4月 v9.0	R181 先天性肾上腺增生携带者检测由靶向变异检测改为单基因测序
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R388	先天性肾上腺连锁检测增生 已退役 CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R154	R154 低磷血症或佝偻病 在ALP偏低的情况下对资格标准的补充。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R223	R223 遗传性嗜铬细胞瘤和副神经节瘤(不包括NF1) 从标准6中移除。肾细胞癌(任何年龄)
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R158	R158 脂肪营养不良——儿童期发病 CI 名称改为严重胰岛素抵抗和脂肪营养不良综合征。检测资格标准中删除了儿童期起病的要求。 在标准中纳入了严重胰岛素抵抗。

Date	Document Name	Version	Summary of Changes
			Added gene targets to the panel.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R293 Albright hereditary osteodystrophy, pseudohypoparathyroidism, pseudopseudohypoparathyroidism, acrodysostosis and osteoma cutis Removed MLPA test type R29.3 as STX16 testing now include in R29.2 Added Paediatrics as a requesting specialty
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R445 Common aneuploidy testing - NIPT Changed CI name TO: T21, T18 and T13 common aneuploidy testing - NIPT Included in the testing criteria full name of trisomy 21, 18 and 13 Aligned criteria with R470
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R470 T21, T18 and T13 common aneuploidy testing – NIPT NHS Fetal Anomaly Screening Programme (FASP) New CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R318 Recurrent miscarriage with products of conception available for testing Removed R297 as an overlapping clinical indication as R297 has been retired (see separate entry) and added R464 Recurrent miscarriage where products of conception are not available for testing - parental karyotype, as a new overlapping Clinical Indication.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R22 Fetus with a likely chromosomal abnormality Error correction on 3rd bullet point of testing criteria to specify intrauterine death.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v	R306 Apert 综合征的 NIPD——变异检测 R307 伴黑棘皮病的 Crouzon 综合征 NIPD——变异检测 R308 FGFR2 相关颅缝早闭综合征的 NIPD——变异检测 R309 FGFR3 相关骨骼发育不良的 NIPD——变异检测 从标准中删除既往妊娠曾患该病且变异已确认的情况。
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R304 NIPD for cystic fibrosis - haplotype testing Error correction: removed “where parents are not consanguineous”
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R433 NIPD for Monogenic diabetes, subtype glucokinase Amended name of CI to: Non invasive prenatal testing for Monogenic diabetes, subtype glucokinase
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R175 Pancreatitis Removal of R175.2 as PRSS1 can now be analysed off the panel test R175.1.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R177 Hirschsprung disease Retired CI

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			已向检测面板添加基因靶点。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R293 奥尔布赖特遗传性骨营养不良， 假性甲状旁腺功能减退症， 假性假甲状旁腺功能减退症、肢端发育不全和皮肤骨瘤 已移除 MLPA 检测类型 R29.3，因为 STX16 检测现已纳入 R29.2 新增儿科作为申请专科
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R445 常见非整倍体检测 - NIPT 将CI名称更改为： T21、T18 和 T13 常见非整倍体检测 - NIPT 检测标准中纳入21、18和13三体的全称 与R470对齐的标准
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R470 T21、T18和T13常见非整倍体 testing - NIPT NHS 胎儿异常筛查计划(FASP) 新 CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R318 复发性流产伴妊娠物 可进行受孕检测 删除 R297 作为重叠临床指征，因为 R297 已停用(见单独条目)，并新增 R464 复发性流产且无流产组织可供检测--父母核型分析，作为新的重叠临床指征。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R22 胎儿可能存在染色体异常 对检测标准第3个项目符号进行错误更正，以明确宫内死亡
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R306 Apert 综合征的 NIPD——变异检测 R307 伴黑棘皮病的 Crouzon 综合征 NIPD——变异检测 R308 FGFR2 相关颅缝早闭综合征的 NIPD——变异检测 R309 FGFR3 相关骨骼发育不良的 NIPD——变异检测 从标准中删除既往妊娠曾患该病且变异已确认的情况。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R304 囊性纤维化的NIPD--单倍型检测 更正：删除了“where parents are not 近亲”
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R433 单基因糖尿病的 NIPD，亚型 葡萄糖激酶 CI 名称修改为：单基因糖尿病(葡萄糖激酶亚型)的无创产前检
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R175 胰腺炎 移除 R175.2，因为 PRSS1 现在可通过 panel 检测 R175.1 i
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R177 先天性巨结肠症 已停用CI

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April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R438 Paediatric pseudo-obstruction syndrome Due to retirement of R177, added to where in the pathway: This test should be used where testing for Hirschsprung disease is required.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R258 Cytopenia - Fanconi breakage testing indicated 已退役 CITT R258.3 MLPA，因为 CNV 可通过 panel 检测 R258.2 进行分析。
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R208 Inherited breast cancer and ovarian cancer Error correction: to 4b removal for need for criteria 2 to be met.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R210 Inherited MMR deficiency (Lynch syndrome) Amended wording in the Lynch related cancers for sebaceous adenomas and carcinoma. Added Dermatology as a requesting specialty Change to the wording above the associated tests table to: Please note that not all the associated tests will be undertaken in every case. The clinical presentation will indicate the tests that are necessary
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R211 Inherited polyposis and early onset colorectal cancer - germline test Addition to requesting specialties: Gynaecology
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R414 APC Associated Polyposis Amendment to criterion 7 and addition of criterion 8. Removal of R359 Childhood solid tumour panel, from overlapping clinical indications as R359 has been retired, see separate entry for the details. Addition to requesting specialties: Dermatology
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R215 Hereditary diffuse gastric cancer Amendment to criterion 1e, 1g and 1h
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R220 Wilms tumour with features suggestive of predisposition Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R358 Familial rhabdoid tumours Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R359 Childhood solid tumours Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R456 Embryonal tumour of possible germline origin New CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R457 Sarcoma of possible germline origin New CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R224 Inherited renal cancer Amendments to criteria 2. And 6.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R254 Familial melanoma Amendments to testing criteria

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2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R438	R438 儿童假性肠梗阻综合征 由于 R177 停用，在路径中的适用位置新增：当需要进行先天性巨结肠症检测时应使用本检测。
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R258	R258 血细胞减少 - Fanconi断裂检测指示的 已退役 CITT R258.3 MLPA，因为 CNV 可通过 panel 检测 R258.2 进行分析。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R208	R208 遗传性乳腺癌和卵巢癌 错误更正：针对4b，删除关于需要满足标准2的要求。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R210	R210 遗传性MMR缺陷(Lynch综合征) 修改 Lynch 相关癌症中皮脂腺瘤和皮脂腺癌的措辞。 新增皮肤科为申请科室将相关检测表格上方的措辞改为： 请注意，并非所有相关检测都会在每个病例中进行。临床表现将指示必要的检测
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R211	R211 遗传性息肉病及早发性结直肠癌--胚系检测 申请专科补充：妇科
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R414	R414 APC相关息肉病 修订标准 7 并新增标准 8。从重叠临床指征中删除 R359 儿童实体瘤 panel，因为 R359 已停用，详情见单独条目。申请科室新增：皮肤科
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R215	R215 遗传性弥漫性胃癌 对标准1e、1g和1h的修订
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R220	具有提示性特征的肾母细胞瘤易感性 已退役 CI
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R358	家族性横纹肌样肿瘤 已停用CI
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R359	儿童实体瘤 已停用CI
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R456	可能源于生殖系的胚胎性肿瘤 新增CI
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0 R457	可能源于生殖系的肉瘤 新增CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R224	R224 遗传性肾癌 对标准2和标准6的修订。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R254	R254 家族性黑色素瘤 检测标准的修订

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April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R365 Fumarate hydratase-related tumour syndromes Amendment to criterion b.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R444 NICE approved PARP inhibitor treatment Amendment to criteria 3. And 4 for R444.1. Due to change in CDF eligibility criteria for OLAP 6 (adjuvant olaparib in patients with high risk ER positive HER2 negative breast cancer).
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R450 Diagnostic testing for Isovaleric acidaemia Removal of text in the criteria: In the case of isovaleric acidaemia, this means that testing is almost exclusively used at those in whom biochemical results indicate a likely pseudodeficiency allele is present. Confirming in the criteria that genetic testing is only where required as part of the diagnostic testing pathway.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R315 POLG-related disorder Removal of R59 as overlapping clinical indication as R59 is retired. Addition of R27 as an overlapping Clinical Indication with note that this should be used, or other relevant broader test, where clinical features are not strongly suggestive of POLG-related disorder and a broader differential diagnosis is under consideration.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R297 Possible structural chromosomal rearrangement - karyotype or Targeted Chromosomal Analysis Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	New CIs created due to retirement of R297 R463 Cytogenetic characterisation of a genomic abnormality – Karyotype or Targeted Chromosome Analysis R464 Recurrent miscarriage, products of conception not available – parental karyotype R465 Familial cytogenetic rearrangement - Karyotype or Targeted Chromosome Analysis R466 Unexplained infertility – karyotype R467 Gamete donors – karyotype R468 Possible sex chromosome aneuploidy or structural rearrangement – Targeted Chromosome Analysis
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R298 Possible structural or mosaic chromosomal abnormality – FISH Removal of R297 as an overlapping Clinical Indication as this has been retired. Addition of two new Clinical Indications in overlapping Clinical Indications; R463 and R465.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R104 Skeletal dysplasia

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2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R365 富马酸水合酶相关肿瘤综合征 对标准b的修订。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R444 NICE 批准的 PARP 抑制剂治疗 修订 R444.1 的标准 3 和 4。由于 OLAP 6(高危 ER 阳性 HER2 阴性乳腺癌患者的辅助奥拉帕利)的 CDF 检测资格标准发生变化。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R450 异戊酸血症的诊断检测 删除标准中的文字：对于异戊酸血症，这意味着检测几乎仅用于生化结果提示可能存在假性缺陷等位基因的患者。 在标准中确认基因检测仅在作为诊断性检测的一部分有需要时进行 通路。
2026年4月 罕见与遗传性	疾病检测资格标准 2026年4月	2026年4月 v9.0	R315 POLG相关疾病 删除 R59 作为重叠临床指征，因为 R59 已停用。新增 R27 作为重叠临床指征，并注明当临床特征不强烈提示 POLG 相关疾病且正在考虑更广泛的鉴别诊断时，应使用本检测或其他相关的更广泛检测 考虑。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R297 可能的染色体结构异常 重排 - 核型分析或靶向染色体分析 已退役 CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	因 R297 停用而新增的 CI R463 基因组异常的细胞遗传学特征分析--核型分析或靶向染色体分析 分析 R464 复发性流产，无流产组织样本--父母核型分析 R465 家族性细胞遗传学重排--核型分析或靶向染色体分析 R466 不明原因不孕--核型分析 R467 配子捐献者--核型分析 R468 可能的性染色体非整倍体或结构重排--靶向染色体分析 分析
2026年4月 罕见与遗传性	疾病检测资格标准 2026年4月	2026年4月 v9.0	R298 可能的染色体结构异常或嵌合体异常 – FISH 删除R297作为重叠临床指征，因为该指征已停用。在重叠临床指征中新增两个新临床指征：R463 和 R465。
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R104 骨骼发育不良

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			Addition to criteria stating that isolated short stature, without evidence of an underlying abnormality of the bones is not appropriate to test via this indication. Please see overlapping indications for tests that may be more appropriate in these cases. Addition of overlapping CIs: R453 Monogenic short stature R52 Short stature – SHOX deficiency Addition of requesting specialties: • Paediatrics • Endocrinology
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R415 Cleidocranial Dysplasia (CCD) Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R101 Ehlers Danlos syndrome with a likely monogenic cause Addition to the testing criteria to support appropriate requesting of testing. Addition to overlapping CIs: R125 and links to the HSS for Ehlers Danlos
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R102 Osteogenesis imperfecta Clarification in the criteria provided: Referrals where non-accidental injury is suspected should be discussed with the OI Highly Specialised Service before requesting genomic testing
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R284 Van der Woude syndrome Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R471 Neurodegenerative Disorders, adult onset – Prenatal Exclusion Testing New CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R58 Adult onset neurodegenerative disorder Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	New CIs replacing R58: R458 Young onset or familial dementia R459 Young onset or complex Parkinson disease R460 Amyotrophic lateral sclerosis R461 Cerebral amyloid angiopathy
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	A new super panel of gene targets created so that the gene targets for the following CIs are all the same: R54 Hereditary ataxia with onset in adulthood R56 Adult onset dystonia, chorea or related movement disorder R458 Young onset or familial dementia R459 Young onset or complex Parkinson disease R460 Amyotrophic lateral sclerosis R461 Cerebral amyloid angiopathy R60 Adult onset hereditary spastic paraplegia The new super panel on panelapp is called

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			在标准中新增说明：孤立的矮身材，无潜在骨骼异常证据者，不适合通过本指征进行检测。对于这些情况可能更合适的检测，请参见重叠指征。新增重叠 CI:R453 单基因矮身材 R52 矮小症 - SHOX 缺陷新增申请专科： • 儿科 • 内分泌学
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R415 锁骨颅骨发育不良(CCD) 已停用CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R101 埃勒斯-当洛斯综合征，可能由单基因病因引起 对检测标准的补充，以支持适当地申请检测。 补充至重叠 CI:R125 及指向 Ehlers Danlos HSS 的链接
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R102 成骨不全症 对所提供的标准作出澄清： 怀疑非意外伤害的转诊应在申请基因组检测前与 OI 高度专业化服务团队讨论
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R284 Van der Woude 综合征 已停用CI
2026年4月	罕见病与遗传病 疾病检测资格标准 2026年4月	2026年4月 v9.0	R471 神经退行性疾病，成人起病 - 产前排除性检测 新增CI
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R58 成人起病神经退行性疾病 已停用CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	新增 CI，替代 R58: R458 早发型或家族性痴呆 R459 青年起病或复杂性帕金森病 R460 肌萎缩侧索硬化 R461 脑淀粉样血管病
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	新建基因靶标超级panel，以便以下CI的基因靶点均为相同： R54 成年起病的遗传性共济失调成年起病的肌张力障碍、舞蹈症或相关疾病 R56 成年起病的遗传性共济失调成年起病的肌张力障碍、舞蹈症或相关疾病 运动障碍 R458 早发型或家族性痴呆 R459 青年起病或复杂性帕金森病 R460 肌萎缩侧索硬化 R461 脑淀粉样血管病 R60 成人起病遗传性痉挛性截瘫 panelapp 上新的超级面板叫做

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			Adult-onset neurological disorders. The panelapp ID is 1669. The CI names in the Test Directory will remain as they currently are.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	Confirmatory STR CITT for the following neurology CIs has been removed as the confirmation testing code R443 should be used instead: R56.4 Adult onset dystonia, chorea or related movement disorder R60.4 Adult onset hereditary spastic paraplegia R84.5 Cerebellar anomalies R57.6 Childhood onset dystonia, chorea or related movement disorder R61.5 Childhood onset hereditary spastic paraplegia R54.5 Hereditary ataxia with onset in adulthood R55.5 Hereditary ataxia with onset in childhood R78.6 Hereditary neuropathy or pain disorder R381.4 Other rare neuromuscular disorders
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R59 Early onset or syndromic epilepsy Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R378 Linkage testing for Duchenne or Becker muscular dystrophy Retired CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R82 Limb girdle muscular dystrophies, myofibrillar myopathies and distal myopathies Addition to where in the pathway to signpost to the HSS
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R85 Holoprosencephaly – NOT chromosomal Change in CI name to: Holoprosencephaly Amendments to testing criteria and where in the pathway. Addition of overlapping CIs: R27, R89, R26 and R28.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R221 Familial tumours of the nervous system Amendments to the testing criteria
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R222 Neurofibromatosis type 1 Addition of criteria 8. And 9.: 8. Axillary/inguinal freckling 9. Malignant Peripheral Nerve Sheath Tumour
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R337 CADASIL Removal of R58 from overlapping Clinical Indications. Addition of R461 Cerebral amyloid angiopathy as an overlapping Clinical Indication where a broader differential diagnosis is under consideration.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R190 Pneumothorax – familial Amendment to testing criteria
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R192 Surfactant deficiency Retired CI

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			成年起病的神经系统疾病。panelapp ID 为 1669。检测目录中的 CI 名称将保持现状不变。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	针对以下神经病学指征的确证性 STR CITT 已删除 CI，因为应改用确认检测代码 R443: R56.4 成人起病的肌张力障碍、舞蹈症或相关运动障碍 R60.4 成人起病遗传性痉挛性截瘫 R84.5 小脑异常 R57.6 儿童期起病的肌张力障碍、舞蹈症或相关运动障碍 R61.5 儿童期起病遗传性痉挛性截瘫 R54.5 成年起病的遗传性共济失调 R55.5 儿童期起病的遗传性共济失调 R78.6 遗传性神经病或疼痛障碍 R381.4 其他罕见神经肌肉疾病
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R59 早发性或综合征性癫痫 已停用CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R378 杜氏或贝克型肌营养不良症的连锁检测 肌营养不良 已退役 CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R82	R82 肢带型肌营养不良症， 肌原纤维肌病和远端肌病在路径中的适用位置新增指引至 HSS
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R85	R85 前脑无裂畸形——非染色体性 CI 名称改为：前脑无裂畸形修订检测标准及路径中的适 通路。 重叠置信区间(CI)的添加：R27、R89、R26 和 R28。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R221	R221 家族性神经系统肿瘤 检测标准的修订
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R222	R222 1型神经纤维瘤病 增加标准8和9： 8. 腋窝/腹股沟雀斑 9. 恶性外周神经鞘瘤
2026年4月	罕见病与遗传病 疾病检测资格标准 2026年4月	2026年4月 v9.0	R337 CADASIL 腋窝/腹股沟雀斑 适应症。恶性外周神经鞘瘤 从重叠临床中移除 R58 新增R461脑淀粉样血管病作为重叠临床指征，适用于正在考虑更广泛鉴别诊断的情况。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0 R190	R190 气胸——家族性 检测标准修订
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R192 表面活性物质缺乏症 已停用CI

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April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R462 Childhood interstitial lung disease New CI
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R239 Incontinentia pigmenti Addition to criteria specifying IKBKG-related immunodeficiency. Added to requesting specialties: Immunology (+/- Paediatrics).
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R89 Ultra-rare and atypical monogenic disorders Addition to criteria: Requests that include any panel for inherited cancers must be taken to the UKCGG/CanGene-CanVar National Multidisciplinary team meeting and receive delegate approval to proceed.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R370 Validation test FROM: Validation test TO: Validation of unaccredited findings Amended testing criteria to: Validation of the presence, and clinical interpretation, of a genomic variant detected outside of an accredited process (e.g. from research findings) when required for diagnostic reporting.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R443 Confirmation test Amended testing criteria to clarify when this test should be used. Amended requesting specialties by removing clinical genetics and keeping only genomics laboratory as the requesting specialty.
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R409 Linkage testing for other recognisable Mendelian disorders Amended name of CI to: Linkage testing for recognisable Mendelian disorders Removed: “where linkage testing is not facilitated via an alternative clinical indication”
April 2026	Rare and Inherited Disease eligibility criteria April 2026	April 2026 v9.0	R447 Diagnostic discovery – validation/confirmation Amended name of CI to: Validation of WGS Diagnostic discovery

日期	文档名称	版本	变更摘要
2026年4月	罕见病与遗传病 2026年4月资格标准	2026年4月 v9.0	R462 儿童间质性肺病 新增CI
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R239 色素失禁症 补充 IKBKG 相关标准 免疫缺陷。 已添加至申请专科：免疫学(+/- 儿科)。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R89 超罕见与非典型单基因疾病 标准补充： 包含任何遗传性癌症检测面板的申请必须提交至UKCGG/CanGene-CanVar全国多学科团队会议，并获得代表批准后方可继续进行。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R370 验证测试 来自：验证测试 致：未获认可发现的验证修订后的检测标准 为： 对在认可流程之外检测到的基因组变异(例如来自研究发现)的存在性及临床解读进行验证，前提是诊断报告需要。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R443 确认检测 修订了检测标准，以明确该检测应在何时使用。 修订申请科室，移除临床遗传学，仅保留基因组实验室作为申请科室。
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R409 针对其他可识别疾病的连锁检测 孟德尔遗传病 将 CI 的名称修改为：可识别孟德尔病的连锁检测 已移除：“当连锁检测未通过替代临床指征促进时”
2026年4月	罕见病与遗传病 检测资格标准 2026年4月	2026年4月 v9.0	R447 诊断发现--验证/确认 将 CI 的名称修改为：WGS 诊断发现的验证

425 20th May 2026 v9.1

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