

Identifying Glucokinase Hyperglycaemia from gestational diabetes

A resource for midwives

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Project Midwives for Monogenic Diabetes, East Genomics

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Monogenic diabetes: Overview

What is monogenic diabetes?

- A form of diabetes caused by a **single gene variant** (mono=one; genic=gene).
- Often referred to as Maturity Onset Diabetes of the Young (MODY).

Key features





- Usually diagnosed **before age 25** and often seen in people with a **normal BMI**
- Autosomal dominant inheritance (50% chance **for each child** to inherit the variant)
- There are many MODY subtypes, but the four most common: **GCK, HNF1A, HNF4A and HNF1B**



If suspected in pregnancy

- Discuss genetic testing with the endocrine team
- Eligibility criteria is available in the [National Genomic Test Directory](#)

Common MODY Subtypes: Key Features for Midwives

MODY Type	Gene Function	Typical Presentation	Progression	Treatment Outside Pregnancy	Pregnancy Considerations	Key Distinguishing Features	Find out more
GCK-MODY	Glucose “sensor” sets a higher threshold for insulin release	Mild, stable fasting hyperglycaemia from birth	Non-progressive	No treatment needed	Management depends on fetal genotype	Benign, stable hyperglycaemia	 What is Glucokinase (GCK)? // Diabetes Genes
HNF1A-MODY	Transcription factor affecting insulin production	Young-onset diabetes (teens/twenties)	Progressive	Very sensitive to sulfonylureas (SU)	Discuss genetic testing with endocrine team	Most common MODY; high SU sensitivity	 Hepatic Nuclear Factor 1 Alpha (HNF1A) // Diabetes Genes
HNF4A-MODY	Similar role to HNF1A in insulin production	Young-onset diabetes	Progressive	Sensitive to SU	Macrosomia & neonatal hypoglycaemia; discuss genetic testing	Parent often has diabetes; neonatal hypoglycaemia	 Hepatic Nuclear Factor 4 Alpha (HNF4A) // Diabetes Genes
HNF1B-MODY	Transcription factor important in kidney & pancreas development	Diabetes age 10–47; often with renal anomalies	Variable; often linked to renal decline	Often insulin-dependent; SU usually ineffective	Fetal renal cysts may be seen on ultrasound	Renal cysts, uterine/genital anomalies, gout, abnormal LFTs, low magnesium	 HNF1B MODY & RCAD // Diabetes Genes

Identifying Glucokinase Hyperglycaemia (GCK-MODY) from gestational diabetes



Key Facts for Glucokinase hyperglycaemia

- **Glucokinase hyperglycaemia is a benign form of hyperglycaemia**

It is a genetic condition where the glucokinase enzyme has a higher glucose threshold for triggering insulin release. This leads to **lifelong, mild, stable fasting hyperglycaemia**.

- **Glucose levels are stable and non-progressive**

People typically have **fasting glucose 5.5–8 mmol/L** and an **HbA1c of 36–57 mmol/mol**. Levels do not worsen over time.

- **People feel well and have no diabetes-related risks** because glucose levels are only mildly raised and stable:

- No medication is needed
- No routine HbA1c monitoring
- No retinal screening
- No foot checks
- No increased risk of type 2 diabetes

- **Why pregnancy is different**

Fetal growth depends on whether the fetus inherits the glucokinase variant and is why pregnancy management is unique compared with gestational diabetes.

Treatment is only required if the fetus is predicted not to have the gene variant and shows excessive growth.

- **Family testing is not routinely required**

Only consider testing if a relative has been labelled “diabetic” or is planning a pregnancy.



Testing Criteria

When gestational diabetes is diagnosed, it's important to consider whether the pattern of hyperglycaemia could reflect glucokinase hyperglycaemia (GCK-MODY). People with mild, stable fasting hyperglycaemia from early pregnancy may meet the [NHS England » National genomic test directory](#) for monogenic diabetes and should be reviewed to see if testing is appropriate.

*Gestational Diabetes
(in current pregnancy)



*Fasting Blood Glucose (FBG)
5.5 – 8 mmol/L



*BMI <30kg/m² (if White)
or
BMI <27kg/m²
(if from an ethnic group with an
increased chance of type 2 diabetes)

*Criteria correct as of March 2026 please check with the [testing directory](#) for the most up-to-date criteria

Important Note

If the person meets the criteria, which includes a fasting blood glucose (FBG) of 5.5 – 8 mmol/L, **review any previous laboratory FBG results** (if available). **If previous FBG are < 5.5mmol/L, genetic testing is not required**

Completing the referral form

Below are the key details to complete on the referral form (for a GDM patient):

- ✓ **Patient details**
- ✓ **Consent**
- ✓ **Clinical information:** Age at diagnosis, diagnosed during pregnancy, height, weight & current BMI, FBG or OGTT result, HbA1C
- ✓ **Family history** (if any)
- ✓ **Testing required:** 'GCK Sanger sequencing'

MODY calculator, C-peptide & Diabetes Autoantibody panel **are not required** for glucokinase hyperglycaemia testing within the GDM pathway

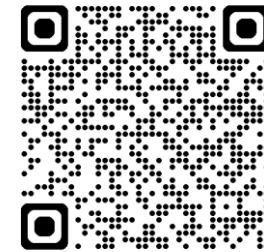
Helpful Resources



[National genomic test directory](#)



[Referral form](#)



[Referral form Support Guide](#)

Management in Pregnancy

In glucokinase hyperglycaemia, fetal growth is determined by whether the fetus inherits the glucokinase variant. Non-Invasive Prenatal Testing (NIPT) can help identify the likely fetal genotype early and guide pregnancy management.

NIPT for the GCK gene change

NIPT analyses cell-free fetal DNA in maternal blood to determine whether the fetus has inherited the known familial glucokinase variant. It is also available for HNF4A.

- Safe, blood-based test
- Reliable from **12 weeks** when fetal fraction is adequate

Sample Requirements:



1

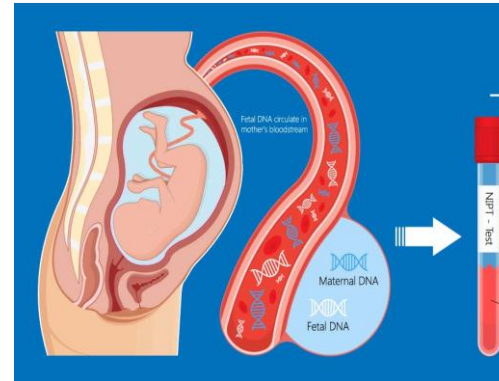
A maternal venous sample

2

A capillary paternal sample

3

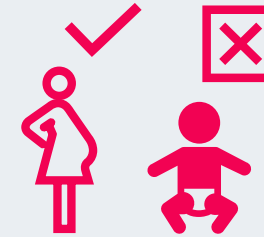
A cord blood sample (once the baby is born)



NIPT is not suitable/appropriate:

- Diagnosis in late gestation of pregnancy (discuss with the laboratory)
- If testing is declined
- Multiple pregnancy
- Biological parent (paternal) sample not available

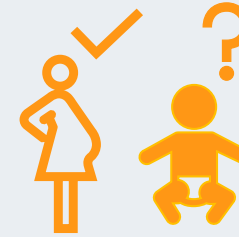
Pregnancy Management Based on Fetal Genotype/NIPT result



Person **with** GCK & Fetus **without** GCK

=
Increased risk of macrosomia

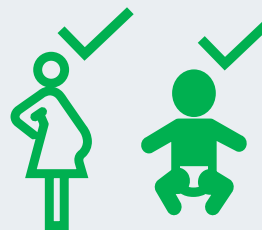
Serial scans; consider insulin if excessive growth develops; consider timing of birth



Person **with** GCK & fetal **genotype unknown**

=
Unknown risk of macrosomia

Serial scans; consider insulin if excessive growth develops; consider timing of birth



Person **with** GCK & Fetus **with** GCK

=
Normal growth expected
No increased risks
No need for insulin during pregnancy



East Genomics

Supporting information & Resources

eastgenomics.nhs.uk

Comparative HbA1c levels

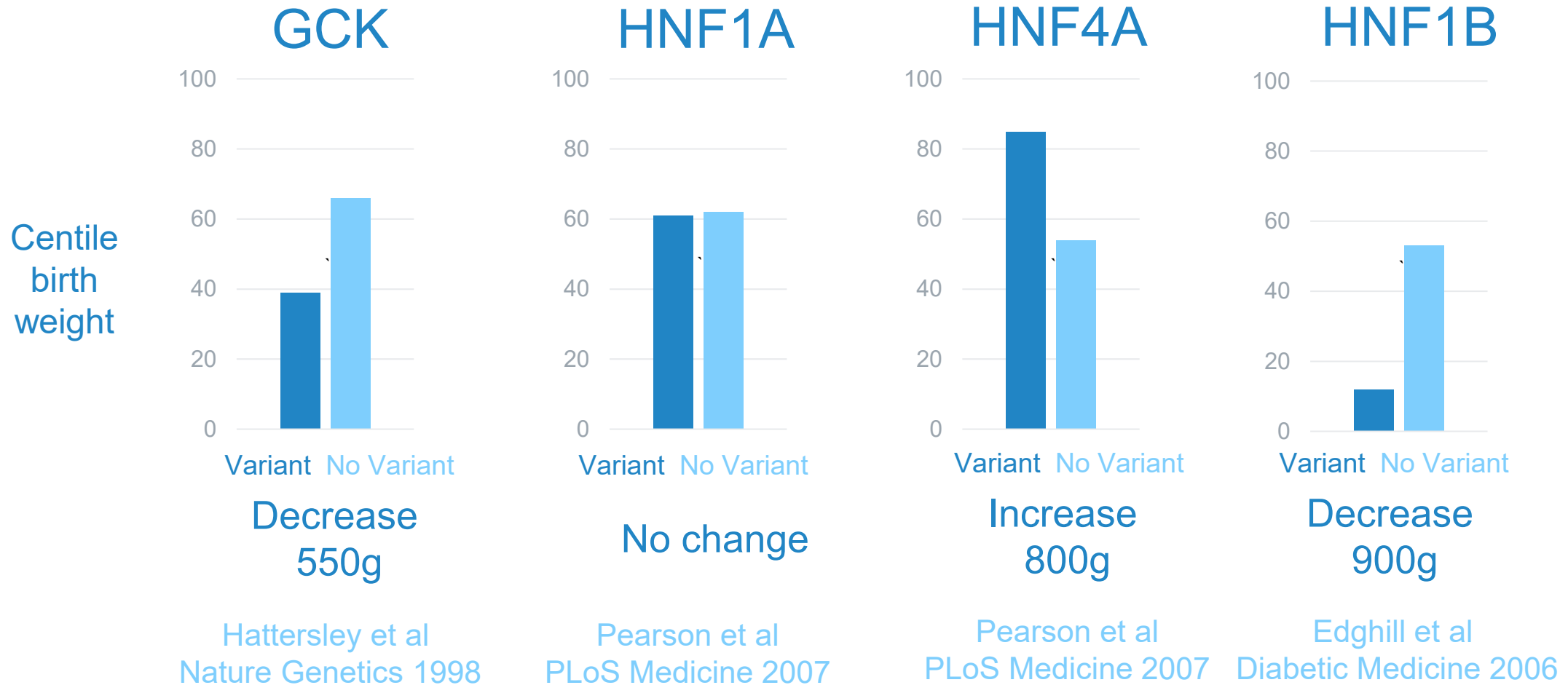
No *GCK* gene variant



GCK gene variant (glucokinase hyperglycaemia)



Birth weight in MODY subtypes reflects fetal beta cell function

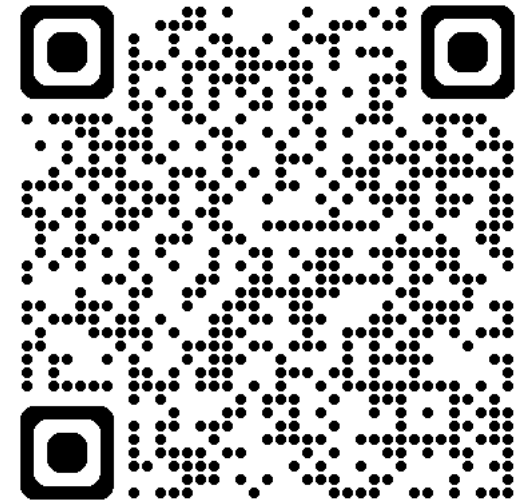


MODY Probability Calculator

Not required if: Glucokinase hyperglycaemia is suspected in pregnancy

Use with caution:

- Close to diagnosis of established diabetes
- Global majority ethnicity
- Patients diagnosed >35 years
- In pregnancy, if undertaking R141 testing



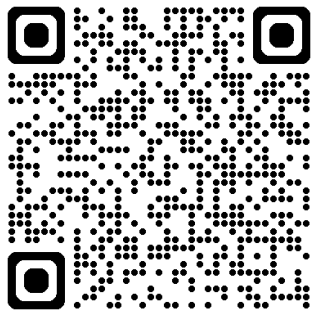
MODY Probability Calculator

Further resources



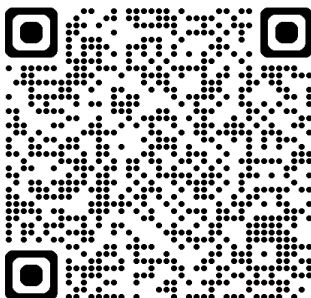
DiabetesGenes.org

Clinical and research resource that provides clear, evidence-based information on genetic forms of diabetes, including MODY, neonatal diabetes, and other rare monogenic types. It supports both patients and healthcare professionals with guidance on diagnosis, testing, and treatment



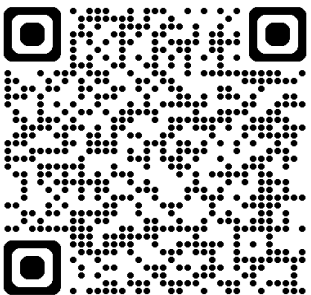
Patient information: Glucokinase hyperglycaemia

A set of patient-friendly leaflets explaining GCK-related hyperglycaemia, its impact on pregnancy, and what a result means for families. Use this resource to direct patients to clear, consistent information and to understand when GCK testing may be relevant.



GeNotes: Genomic notes for clinicians

GeNotes is a quick, practical genetics reference for frontline clinicians, giving clear guidance on when to suspect a genetic condition and how to arrange the right testing including GCK and other forms of MODY



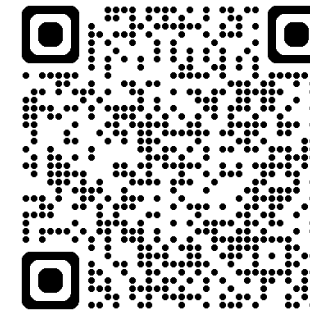
Further Learning



East Genomics e-learning

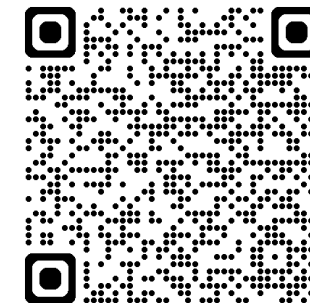
Glucokinase Hyperglycaemia: Rethinking Gestational Diabetes

A guide to recognising GCK-MODY, which often looks like gestational diabetes but needs very different management. Midwives can use this e-learning to understand when to suspect it and how correct identification prevents unnecessary testing and treatment.



Genomics Education Programme: Bitesize Genomics

Short, practical learning modules that help midwives quickly understand key genomic topics relevant to maternity care. Ideal for building confidence in recognising when genomics matters, supporting testing decisions, and guiding patient conversations.



Autosomal Dominant Inheritance

A short animation explaining how autosomal dominant conditions are passed from an affected parent to their child, including the 50% chance of inheritance. A quick, clear resource to help midwives understand and explain basic inheritance patterns during genomic conversations.

