GLUCOKINASE HYPERGLYCAEMIA TESTING WITHIN THE EXISTING PATHWAY FOR GESTATIONAL DIABETES

Template STANDARD OPERATING PROCEDURE (SOP)
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1 INTRODUCTION

This Standard Operating Procedure (SOP) aligns with the national genomic medicine aspirations set out in the *Accelerating genomic medicine in the NHS strategy* (NHS England, 2022) to promote mainstreaming genomic testing within existing services and create sustainable, equitable and effective care pathways. More healthcare professionals are taking responsibility for offering and ordering genetic testing outside of clinical genetics services. This SOP provides the template to standardise the clinical pathway.

This document may use the term pregnant women/people, understanding that practitioners will modify their language in accordance with the preferences of individuals within their care.

What is Monogenic Diabetes/MODY (Maturity Onset Diabetes of the Young)?

Monogenic diabetes is a genetic form of diabetes that is often misdiagnosed as Type 1, Type 2 or Gestational Diabetes (GDM). People with monogenic diabetes have often been diagnosed with diabetes at a young age and have a strong family history of diabetes. There are several subtypes of monogenic diabetes, each with their own clinical features. It is caused by a change (variant) in a single gene and is estimated to be present in 1-2% of people with diabetes in the UK (Diabetes Genes, 2025). Monogenic diabetes is inherited via autosomal dominance, each child of an affected parent with monogenic diabetes has a 50% chance of inheriting the same gene variant (Diabetes Genes, 2025).

Glucokinase (GCK) hyperglycaemia

One of the most common subtypes of monogenic diabetes is Glucokinase Hyperglycaemia (GCK). For people with a variant in their *GCK gene*, stable fasting hyperglycaemia will have been present from birth and does not require any treatment outside of pregnancy. However, during pregnancy the care pathway of maternal hyperglycaemia is determined by the fetal genotype. Pregnant women on a gestational diabetes care pathway have an ideal opportunity to be offered genomic testing for GCK as the diagnosis influences pregnancy management, including fetal growth and risk of macrosomia.

The National Genomic Test Directory outlines the full range of genomic tests that are commissioned for the NHS in England and standardises the criteria for testing. Genetic testing is funded for people who fit the criteria. The test code for glucokinase hyperglycaemia in pregnancy is **R142** (NHS England, 2022). Only patients who meet all 3 criteria are eligible for testing, in accordance with the test directory.

If the diagnosis of GDM has been made via home blood glucose monitoring rather than a laboratory oral glucose tolerance test (OGTT), a laboratory fasting blood glucose should be obtained with a haemoglobin A1C (HbA1c) prior to the offer of genomic testing (Ellard et al, 2000).

If the woman has previous fasting blood glucose results available, these should be reviewed. These samples can be from outside of pregnancy, previous pregnancy or from primary care. If below 5.5 mmol/L, genetic testing would not be required as GCK causes a stable raised fasting hyperglycaemia from birth. If previous HbA1c results, or those in this pregnancy, are available - and lower than 36mmol/mol then do not test. Once eligibility for testing has been confirmed, testing can be offered at any gestation of pregnancy.

Glucokinase hyperglycaemia treatment in pregnancy

Treatment in pregnancy is dependent on the baby's genotype, which can be determined through non-invasive prenatal testing.

Most women with GCK will require no treatment in pregnancy if the baby has inherited the maternal variant in the *GCK* gene, as there is no increased risk of macrosomia. If the baby has not inherited the variant in the *GCK* gene, treatment may be required to reduce the risk of macrosomia. See www.diabetesgenes.org for latest guidance regarding management of pregnancy with GCK (Diabetes Genes, 2025).

2 ROLES AND RESPONSIBILITIES

The responsibility for undertaking this SOP lies with the multidisciplinary maternity diabetes teams, including midwives and diabetes nurses with relevant training. It requires allocation of roles and responsibility for standardising the process for identifying eligibility for testing, arranging testing, communicating diagnosis within the MDT including consideration of maternal medicine specifications e.g. MODY, category B (NHS England, 2021).

3 SPECIFIC STANDARD OPERATING PROCEDURE

1. As pregnant women are diagnosed with GDM, an assessment for eligibility for genomic testing for glucokinase hyperglycaemia should be undertaken (NHS England, 2022).

The National Genomic Test Directory includes the 'Rare and inherited disease eligibility criteria' document which is where eligibility for this test is described.

The test code for glucokinase hyperglycaemia in pregnancy is **R142.**

2. Testing should be offered in a timely manner by a member of the team who is trained and confident in discussing genomic testing. (See **appendix 1** for testing flowchart.) Clinicians may wish to use the **NHS record of discussion form** (see section 4) to aid this discussion, and consent should be recorded in the clinical records. Use of interpreters, language line, or involvement of specialist services may be necessary to ensure understanding and informed choice, in line with Trust guidance.
3. Complete the **R142 MODY genetic referral testing** form electronically and send a copy via e-mail to the Exeter genomics laboratory team. This is then printed and consent signed by the pregnant woman. Include a printed copy with the blood samples.
4. Blood samples should then be taken as per local guidelines, in EDTA tubes, minimum 5ml (same colour bottle as a HbA1c sample).
5. Blood samples should then be sent via local protocol to The Exeter Genomics Laboratory. Continue on GDM pathway until genotype results received.
6. Results will be returned to the requesting clinician/team via NHS secure email system. These should be communicated with the maternity diabetes team and pregnant woman. A copy should be provided to both the pregnant woman and their GP.
7. If no **pathogenic** (disease causing) genetic variant has been identified for the hyperglycaemia (using Sanger sequencing and Next Generation Sequencing), the woman will remain on the gestational diabetes care pathway.
8. If a **pathogenic** or **likely pathogenic** variant in the *GCK gene* is identified, non-invasive prenatal testing can be considered if appropriate.

1. **Non-invasive prenatal testing (NIPT) for fetal genotyping of glucokinase hyperglycaemia:**

The rationale for non-invasive prenatal testing where a maternal *GCK gene* variant has been identified is to influence the management of the pregnancy according to fetal genotype. The baby is at risk of macrosomia if it has **not** inherited the *GCK variant* (Schaefer-Graf, 2004).

Non-invasive prenatal testing:

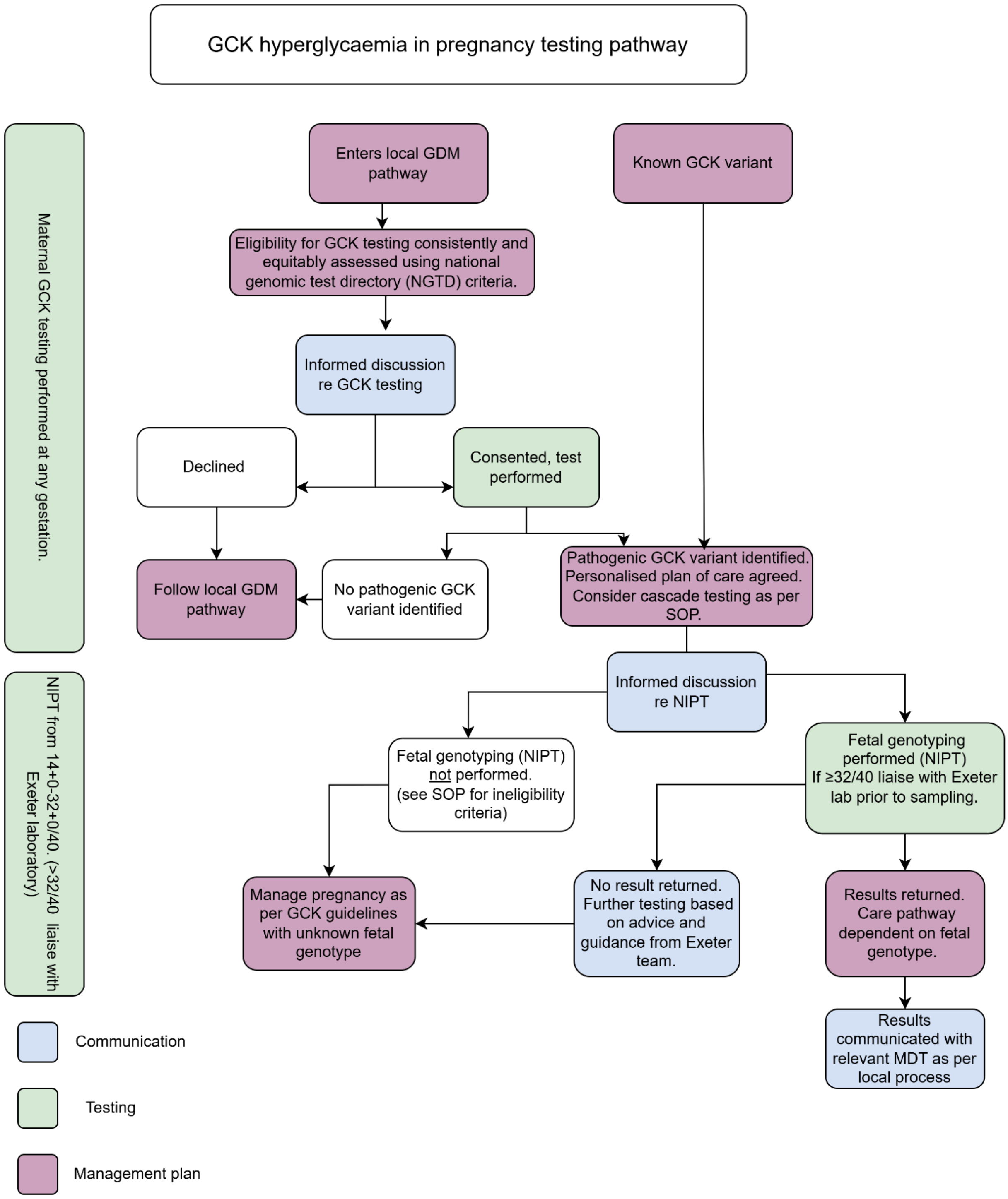
- Can be offered from 14+0 weeks of a singleton pregnancy (not possible in twin or higher order pregnancy), up to 32+0 weeks. After 32+0 weeks gestation, advice should be sought from the Exeter laboratory team to ensure the turnaround time of results will support the management of pregnancy.
- Requires a maternal venous sample in Streck tubes (3 tubes required, provided by Exeter laboratory in testing kit), and paternal capillary sample (please liaise with Exeter laboratory if unable to provide paternal sample).

Documentation of results of NIPT in clinical notes, should be as per local pathway.

All clinical decisions need to be made by the clinicians looking after the pregnant woman, with guidance from the monogenic diabetes team in Exeter if required. In pregnancies, where NIPT is not performed or possible, the woman should continue to be offered treatment on the gestation diabetes pathway (NHS England, 2021).

For latest pregnancy management guidelines, see GCK Guidelines in Pregnancy // Diabetes Genes

4. Appendix 1



GCK hyperglycaemia in pregnancy testing pathway
Maternal GCK testing performed at any gestation.
NIPT from 14+0-32+0/40. (>32/40 liaise with Exeter laboratory)
Enters local GDM pathway
Known GCK variant
Eligibility for GCK testing consistently and equitably assessed using national genomic test directory (NGTD) criteria.
Informed discussion re GCK testing
Declined
Consented, test performed
Follow local GDM pathway
No pathogenic GCK variant identified
Pathogenic GCK variant identified. Personalised plan of care agreed. Consider cascade testing as per SOP.
Informed discussion re NIPT
Fetal genotyping (NIPT) not performed. (see SOP for ineligibility criteria)
Fetal genotyping performed (NIPT) If ≥32/40 liaise with Exeter lab prior to sampling.
Manage pregnancy as per GCK guidelines with unknown fetal genotype
No result returned. Further testing based on advice and guidance from Exeter team.
Results returned. Care pathway dependent on fetal genotype.
Results communicated with relevant MDT as per local process
Communication
Testing
Management plan

5. ASSOCIATED PROCEDURAL DOCUMENTS/FORMS/TEMPLATES

The University of Exeter:

Diabetes Genes > Information for patients and professionals on genetic types of diabetes > Home page

What is Glucokinase (GCK)? // Diabetes Genes

R142 test request form:

Diabetes Genes > Information for patients and professionals on genetic types of diabetes > Genetic Test Referral Forms

Record of discussion form: nhs-genomic-medicine-service-record-of-discussion-form.pdf (england.nhs.uk)

6. REFERENCES

1. NHS England (2022) Accelerating genomic medicine in the NHS 2022.[online] Available from: www.england.nhs.uk/longread/accelerating-genomic-medicine-in-the-nhs/ NHS England » Accelerating genomic medicine in the NHS.

2. Chakera, A.J. Spyer, G. Vincent, N. Ellard, S. Hattersley, A.T. Dunne, F.P. (2014) The 0.1% of the population with glucokinase monogenic diabetes can be recognized by clinical characteristics in pregnancy: the Atlantic Diabetes in Pregnancy cohort. *Diabetes Care.* 37(5): pp1230-1236.

3. Diabetes Genes (2025) What is glucokinase (GCK)? [online]. Available from: https://www.diabetesgenes.org/gck-guidelines-in-pregnancy/ (accessed 11.09.2025).

4. Ellard, S. Beards, F. Allen, L. Shepherd, M. Ballantyne, E. Harvey, R. Hattersley, A.T. (2000) A high prevalence of glucokinase mutations in gestational diabetic subjects selected by clinical criteria. *Diabetologia* 43(2): 250-253.

5. NHS England (2021) Maternal Medicine Network Service Specification. Service specification October 2021. [online]. Available from: NHS England » Maternal medicine networks: service specification accessed 09/09/2025.

6. NHS England (2022). National genomic test directory. [online]. Available from: NHS England » National genomic test directory. Accessed 08/09/2025.

7. Schaefer-Graf UM, Kjos SL, Fauzan OH, Bühling KJ, Siebert G, Bührer C, Ladendorf B, Dudenhausen JW, Vetter K. A randomized trial evaluating a predominantly fetal growth-based strategy to guide management of gestational diabetes in Caucasian women. Diabetes Care. 2004 Feb;27(2):297-302. doi: 10.2337/diacare.27.2.297. PMID: 14747203.