

Monogenic diabetes:

A guideline for NZ healthcare practitioners

Monogenic diabetes refers to single gene disorders resulting in diabetes

- Maternally inherited diabetes and deafness (MIDD) and maturity onset diabetes of the young (MODY) subtypes are thought to account for 1-2% of diabetes cases, and are frequently mistaken for type 1 or 2 diabetes (potentially 2000 cases in New Zealand).
- Neonatal diabetes (ND) diagnosed within 6 months of life is not usually type 1 diabetes and needs genetic testing

Other forms of rare monogenic diabetes, clearly recognisable due to their associated syndromes (eg: Wolfram, Alstrom, Prader-Willi), major disease states (eg: Friedrichs Ataxia, cystic fibrosis) or severe insulin resistance (eg: congenital lipodystrophies, insulin receptor defects) are not included in these guidelines.

Why diagnose MODY, MIDD or ND?

- It changes management
 - No glucose therapy for **GCK** mutations outside of pregnancy
 - Low dose sulphonylurea for **HNF1A** and **HNF4A**
 - Coenzyme Q10 and thiamine for **MIDD**
 - No maternal renal donors in **MIDD** who are obligate carriers of mt.3243A>G
 - Sulphonylurea therapy rather than insulin for **Neonatal diabetes (KCNJ11, SUR1)**
- It improves quality of life by guiding best therapy
- It alters prognosis
 - **GCK** mutations not associated with micro or macrovascular complications
- It alters screening in at risk family members
 - Fasting glucose of 5.5-8mmol/L in **GCK** families
 - Early lowering of renal threshold for glucose in **HNF1A**
 - Early hearing screening for obligate maternal carriers of mt.3243A>G
- It alters management in pregnancy
 - Only 50% of mothers with **GCK** mutations will require insulin during pregnancy if their fetal growth is increased,
 - Babies inheriting **HNF4A** are at increased risk of macrosomia and neonatal hypoglycemia independent of maternal glycaemia or mutation status
- It enables genetic counseling of family members at risk with predictive testing options and management implications for those already diagnosed with diabetes in extended family members
- It can generate opportunities for molecular and clinical research, improving our understanding and management of monogenic diabetes

Phenotypes for common monogenic subtypes

GCK mutations (MODY2) 20-50% MODY cases

- Isolated mild fasting hyperglycaemia
- Small increment on OGTT
- Not associated with micro or macrovascular complications even in the absence of glucose lowering medications
- Absence of family history is common as detected only incidentally or upon screening

HNF1A mutations (MODY3) 20-50% MODY cases

- Progressive beta cell failure commonly presents with hyperglycemia in early adulthood
- Initially elevated post-prandial glucose, with later elevated fasting glucose and marked excursion on OGTT (>4.5 mmol/l)
- Sensitive to **sulphonylureas** e.g. Gliclazide
- Glycosuria with blood glucose < 10 mmol/L
- Elevated HDL

HNF4A mutations (MODY1) 5% MODY cases

- Similar presentation to HNF1A, but with additional neonatal hypoglycemia or macrosomia even without maternal diabetes

HNF1B mutations (MODY5) 5% MODY cases

- Associated with renal cysts, cystic renal dysplasia, glomerulocystic kidney disease,
- Abnormal liver enzymes
- Pancreatic atrophy with exocrine dysfunction

Maternally inherited diabetes and deafness (MIDD)

- Up to 1% of unselected cases of diabetes
- Up to 60% of cases of diabetes associated with sensorineural deafness and maternal family history
- Excess proteinuria, macular retinal dystrophy

Neonatal diabetes (KCNJ11, SUR1, INS)

- Presents from birth to 6 months (1: 200,000 live births)
- Occasional severe associated neurological symptoms
- **Free genetic testing**, may enable oral therapy

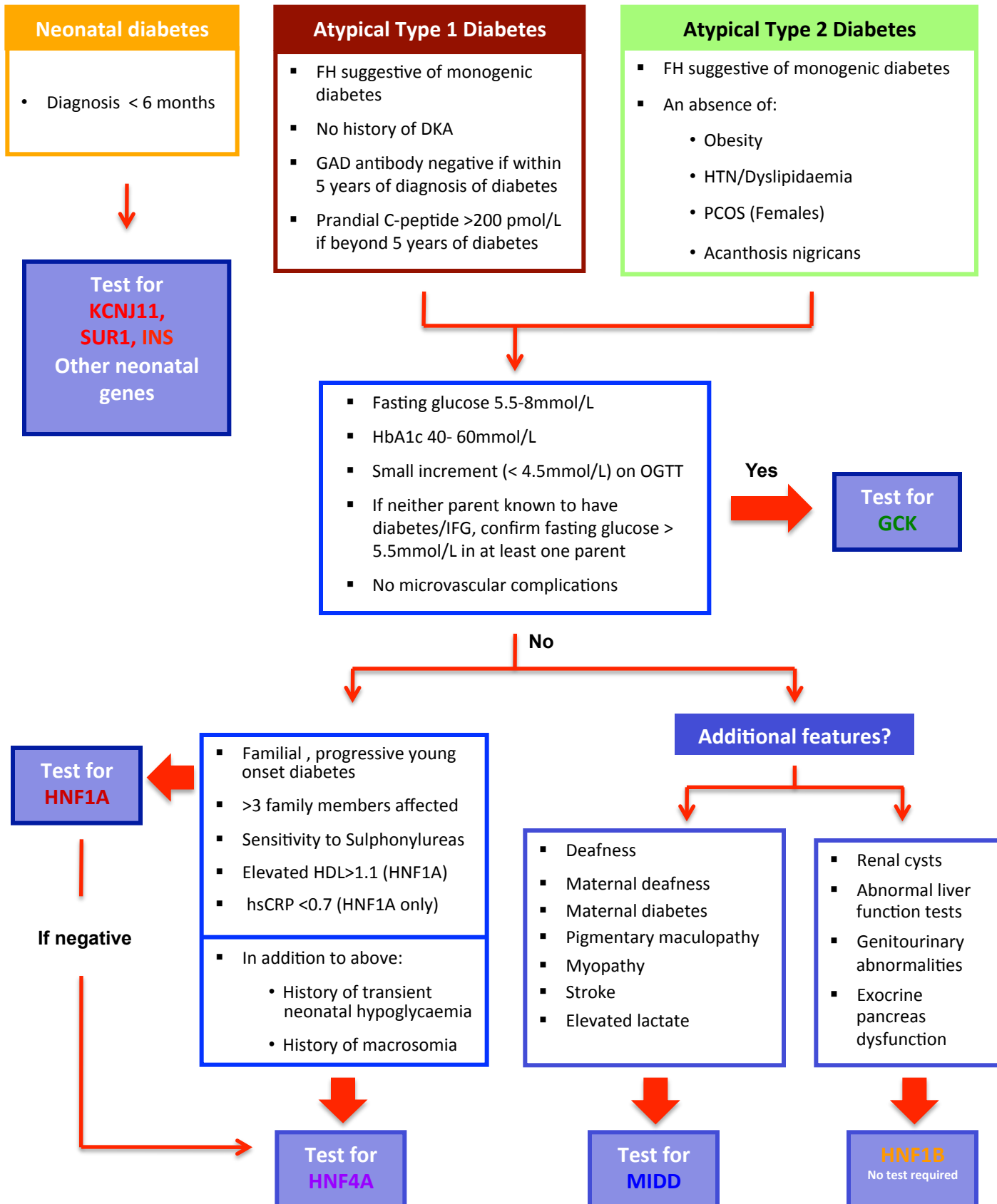
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Diagnostic algorithm for assessment of suspected monogenic diabetes: diabetes diagnosed < 35 yrs



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Procedure and costs

We advise consultant diabetes or endocrinologist review for all molecular genetic testing of suspected cases. Given the expense of these genetic tests it is vital that these tests are used in situations where they are likely to be positive and will alter clinical care. This involves careful clinical selection and physiological tests as appropriate as recommended in form A. Please consider referring all laboratory confirmed probands to regional genetics service for genetic counselling and cascade testing of relatives. Contact R.Murphy@auckland.ac.nz for clinical advice or guideline feedback.

•2 EDTA (purple top) blood samples (minimum 10mL for adults, 5mL for children) are required for **GCK**, **HNF1A**, **HNF4A**, **HNF1B** analysis. Please email completed **form A and B** to the molecular genetics laboratory at Auckland Hospital (molgen@adhb.govt.nz) stating blood samples are on their way via your local laboratory for DNA analysis and attach a copy to your local laboratory form specifying "2 EDTA required for MODY genetic testing at Auckland Hospital".

•2 EDTA (purple top) blood samples (minimum 1mL for neonates) are required for **KCNJ11**, **SUR1**, **INS**, **6q24** and other **neonatal diabetes gene** analysis. Please send 2 EDTA directly to Exeter via your local laboratory to avoid delays in DNA extraction, and prompt testing during neonatal period, using accompanying forms found under neonatal diabetes on www.diabetesgenes.org

•For **MIDD** (mt.3243A>G) tests, specify "DNA for mt.3243A>G analysis" on your local laboratory form, and your local laboratory will send the sample to Canterbury Health Laboratories directly. Buccal cells or urine samples are preferable to blood as the proportion of mutant mitochondrial DNA (heteroplasmy level) is greater in these tissues (highest in muscle).

-**Buccal cells** may be collected using either mouth wash or a dry bacterial swab. Ensure the mouth has been rinsed first if within 2 hours of eating to ensure no food debris is present. Ask the patient to to swish 10mls of sterile water in their mouth for approximately 30 seconds and collect this in a clean container. Or vigorously swab the inside of the cheek approximately 15 times each side. Place the swab in a clean container containing sterile water, seal and send (may need to snap off the long plastic stem).

-**Urinary epithelial cells** collect 20-30mls of early morning urine. DNA yield may depend on how quickly the sample is processed.

Test	Price (NZ\$)	Turnaround time (mths)
GCK	638.88	3
HNF1A	822.00	3
HNF4A	638.88	3
HNF1B	593.10	3
MIDD	621.00	1
Neonatal diabetes genes	Free through Exeter	1

Additional cost for gene deletions analysis using array is \$550, which is currently recommended if suspecting HNF1B as 55% of cases are due to gene deletion. For GCK, HNF1A and HNF4A, gene deletions account for 2% of cases.

Cascade testing of family members for known mutations identified in proband incurs a charge of \$364.14 Please specify proband and mutation (if known) on Form B. Cascade testing is not indicated for MIDD.

Interpretation of genetic test results

Detection of a mutation or gene deletion allows the definite diagnosis of monogenic diabetes to be made. However, failure to detect these does not exclude a diagnosis. Reasons for not detecting a genetic abnormality in patients with a high clinical suspicion of monogenic diabetes could be (1) present laboratory technology is not sufficiently sensitive or specific for detecting all pathogenic mutations or deletions (2) not all causative genes have been identified (3) the index case may not have monogenic diabetes as the currently recognised features are not sufficiently specific for this

Assessing the significance of rare/novel gene variants detected in the index case: Several types of evidence are used to determine the likely pathogenicity of such gene variants (1) searching published literature, epidemiological studies and established databases (2) in vivo functional studies (3) in silico (molecular software) studies. Particular care is required to evaluate novel variants in non-Caucasian ethnic groups. *Ellard, Diabetologia 51: 546-553; 2008*

Diagnostic clues for index case finding

C-peptide: Helpful in distinguishing between T1D or monogenic diabetes as undetectable serum C-peptide usually seen after 5 years of T1D disease duration (DCCT), while persistence of stimulated C-peptide (when glucose is > 8mmol/L) beyond 5 years after T1D >200pmol/L makes T1D unlikely. Recently, persistence of C-peptide in T1D beyond 5 years has been described (*Wang, Diabetes Care 35: 465-470, 2012*) with the majority being below 100pmol/L (1-5% of Type 1D).

Islet autoantibodies: Helpful in discriminating monogenic diabetes from T1D. GAD or IA-2 antibodies remain detectable for many years, with 70% of T1D having either antibody 11 years after diagnosis (*Borg, Acta Paediatr 89: 46-51, 2000*). The prevalence of these antibodies in those with **HNF1A**, **GCK** or **HNF4A** has been found to be the same as in control subjects at 1% (*McDonald, Diabetic Medicine 28: 1028-1033, 2011*)

hsCRP biomarker for HNF1A: the CRP gene has **HNF1A** binding sites in its promoter and low hs-CRP has been seen in **HNF1A** patients compared with other forms of monogenic diabetes such as **HNF4A**, **GCK**, T1D and T2D. The highest discriminatory value of hsCRP is between **HNF1A** and T2D with cut off hsCRP <0.75mg/L showing modest 79% sensitivity and 70% specificity, hence should still be used in combination with clinical characteristics. A lower cut off level <0.55 mg/L achieved a sensitivity of 71% and specificity of 70% for distinguishing between **HNF1A** and **HNF4A**, **GCK**, or **HNF1B**. (*McDonald, Diabetes Care 34: 1860-1862, 2011*). The hs-CRP is not useful if elevated >10 as in the presence of inflammation.

HDL: In the absence of insulin resistance related lowering of HDL characteristic of T2D, the HDL level is moderately discriminatory between **HNF1A** and T2D : plasma HDL > 1.12mmol/L was 75% sensitive and 64% specific at discriminating **HNF1A** from T2D (*McDonald, Clin Chim Acta 18: 927-32, 2012*). HDL levels are similar between **HNF1A**, T1D and healthy controls. Lower HDL levels are seen in **GCK** compared to T1D, and **HNF1A** (animal studies suggest HDL levels may depend on **GCK** activation) *Fendler, Clin Endocrinol 75: 321-7, 2011*.

Management changes

GCK: May stop all glucose lowering therapy (*Murphy, Nat Clin Pract Endocrinol Metab 4: 200-13, 2008*). Once stable glucose is confirmed without glucose lowering therapy (to confirm there is no coincidental additional type of diabetes), blood glucose monitoring is no longer necessary. Screening for microvascular risk may be discontinued. Screening and therapy for cardiovascular risk factors, such as blood pressure, lipids, and HbA1c should be based on traditional individual risk profiles. Predictive or confirmatory genetic testing of family members is generally not required as fasting glucose (>5.5mmol/L) is a good marker of **GCK** status in an affected pedigree. **All women with GCK should be advised to seek referral to diabetes in pregnancy clinic upon pregnancy, as they may require insulin therapy in pregnancy depending on whether their fetus also carries the mutation.** Insulin therapy of maternal hyperglycemia is reserved for those who have accelerated fetal growth during the third trimester (surrogate indication of negative fetal **GCK** mutation). Large insulin doses (at least 0.6-1U/kg) are usually required. Antenatal testing of the fetus for **GCK** mutation is not advised unless CVS or amniocentesis is being performed for another reason.

HNF1A and **HNF4A:** Guidance for transferring patients from insulin to sulphonylureas is available on www.diabetesgenes.org. If predictive testing of **HNF1A** is positive, then screening for glycosuria is better than fasting glucose given the lowered renal threshold in **HNF1A**. Statin therapy in **HNF1A** from age 40 given increased risk of CVD mortality despite elevated HDL, as low ApoM (*Steele, Diabetic Med 27: 157-161, 2010*).

HNF1B: Enables predictive testing of first degree relatives and prompt surveillance for clinical diseases. Almost all have renal disease (hypoplastic glomerulocystic kidney disease, cystic renal dysplasia, solitary functioning kidney, horseshoe kidney, renal cysts) often found in children within the first year of life. De novo cases are common (without family history). Other associated features are diabetes, pancreatic atrophy (often sub-clinical exocrine deficiency), urogenital abnormalities, gout and abnormal liver enzymes. Early insulin therapy is needed.

MIDD (Mt.3243A>G): Avoid metformin. Thiamine (50mg daily) and coenzyme Q10 (150mg daily) supplementation may be helpful (*Suzuki, Diabetologia 41: 584-8, 1998*). Predictive or cascade genetic testing of family members is not recommended as almost all maternal relatives will have obligate carrier status and level of heteroplasmy (mutation load) in peripheral tissues is not useful in predicting clinical course. (*Murphy, Diabet Med 25 (4): 200-13, 2008*)

KCNJ11 and **SUR1:** Guidance for transferring neonatal diabetes patients from insulin to sulphonylureas is available on www.diabetesgenes.org

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Detection of index cases and subsequent family tracing

The key diagnostic challenge in monogenic diabetes is the systematic detection of index cases (first individual diagnosed with monogenic diabetes in the family). Once an index case has been identified, this is the starting point for family tracing or cascade genetic testing by which the majority of monogenic diabetes cases can be efficiently detected.

Co-ordinated **cascade testing** should be organized through referral of the index case to the genetics service with joint collaboration with the diabetes service (contact Genetic Health Service NZ: Central and Southern Hub toll free 0508 364 436 or Northern Hub toll free 0800 476 123). Genetic testing of an individual without diabetes in a family is known as “**predictive**” testing, while in those already known to have diabetes this is known as “**diagnostic**” testing. Risk notification, informing first and then second degree relatives that (1) they are at risk of monogenic diabetes (2) this type of diabetes may have implications for their diabetes therapy and general health (3) genetic testing is available to clarify if they do or do not have monogenic type of diabetes is important. All cases detected in this way will become probands for risk notification of their own first and second degree relatives.

Insurance cover and genetic testing: All individuals with potential monogenic diabetes should be made aware and understand the implications of genetic testing for certain types of insurance cover. Family and personal history of diabetes is currently utilised by insurance companies to make decisions about exclusion of specific conditions from insurance coverage and amount of insurance policy premiums. Genetic confirmation of **GCK** diabetes with no excess risk of microvascular complications is likely to lower insurance premiums based on supporting documentation from a diabetes specialist.

Cost effectiveness of genetic testing

Genetic testing becomes more cost effective as the cost of the test decreases, the likelihood of detecting a monogenic cause increases, if monogenic diagnosis results in cost savings or other benefits in patient health care.

Neonatal diabetes: 40% of those diagnosed between 0 and 6 months and only 1-2% of those diagnosed between 6-12 months have a mutation in **KCNJ11** or **ABCC8**. More than 90% of those with **KCNJ11** or **ABCC8** mutations are able to transfer from insulin to lifelong sulphonylurea therapy and such conversions are associated with improvement in HbA1c sustained over many years reducing concomitant microvascular complications. Currently with free genetic testing through Exeter, this is a cost-neutral to potentially cost-saving test. Even with an initial cost of genetic testing of US \$2815 (and 4 day cost of inpatient transfer of insulin to sulphonylurea therapy and assuming HBGM decline from 6 tests per day to 3 tests per day, the decline in expected probability of microvascular complications from an assumed lifetime mean HbA1c of 8.1% to 6.4% is estimated to becoming cost saving by 10 years and increasing thereafter (*Greeley, Diabetes Care 34: 622-7; 2011*).

GCK, HNF1A and HNF4A: A study simulated diabetes costs and complications in incident cases of diabetes diagnosed in a hypothetical population aged 20-40 years. Modeled variables were based on assumed T2D diagnosis and included complications data from the UKPDS, and underlying 2% MODY in the population (35% with **GCK**, 65% with **HNF1A** or **HNF4A**) based on a one time genetic testing cost of US\$2000 (all 3 genes tested without phenotype discrimination). The genetic testing model assumed that 75% of those with **HNF1A** or **HNF4A** would be treated with sulphonylureas and that all patients with **GCK** would discontinue therapy. Genetic testing was demonstrated to be cost-saving as pick up rate increased to 20% (*Naylor, ADA 2012 oral abstract*).

Our NZ guidelines for genetic testing recommends consideration of individual genetic tests for non-neonatal monogenic diabetes based on clinical grounds, aiming to increase the systematic detection of index cases with a pick up rate of 20%.

Monogenic diabetes database

Please ask all patients you refer for monogenetic testing (regardless of test result outcome) for permission to be included in the monogenic diabetes database, and if agreeable, scan and email forms A, B and signed consent forms (adult or child forms appended) to R.Murphy@auckland.ac.nz or post to Dr Rinki Murphy, FMHS, University of Auckland, Private Bag 92019, Auckland 1142

The purpose of the monogenic diabetes database is to audit and improve NZ diabetes genetic testing guidelines and to enable contact with referring doctors and their patients with recent developments in monogenic diabetes diagnosis and management or relevant research opportunities.

Monogenic diabetes:

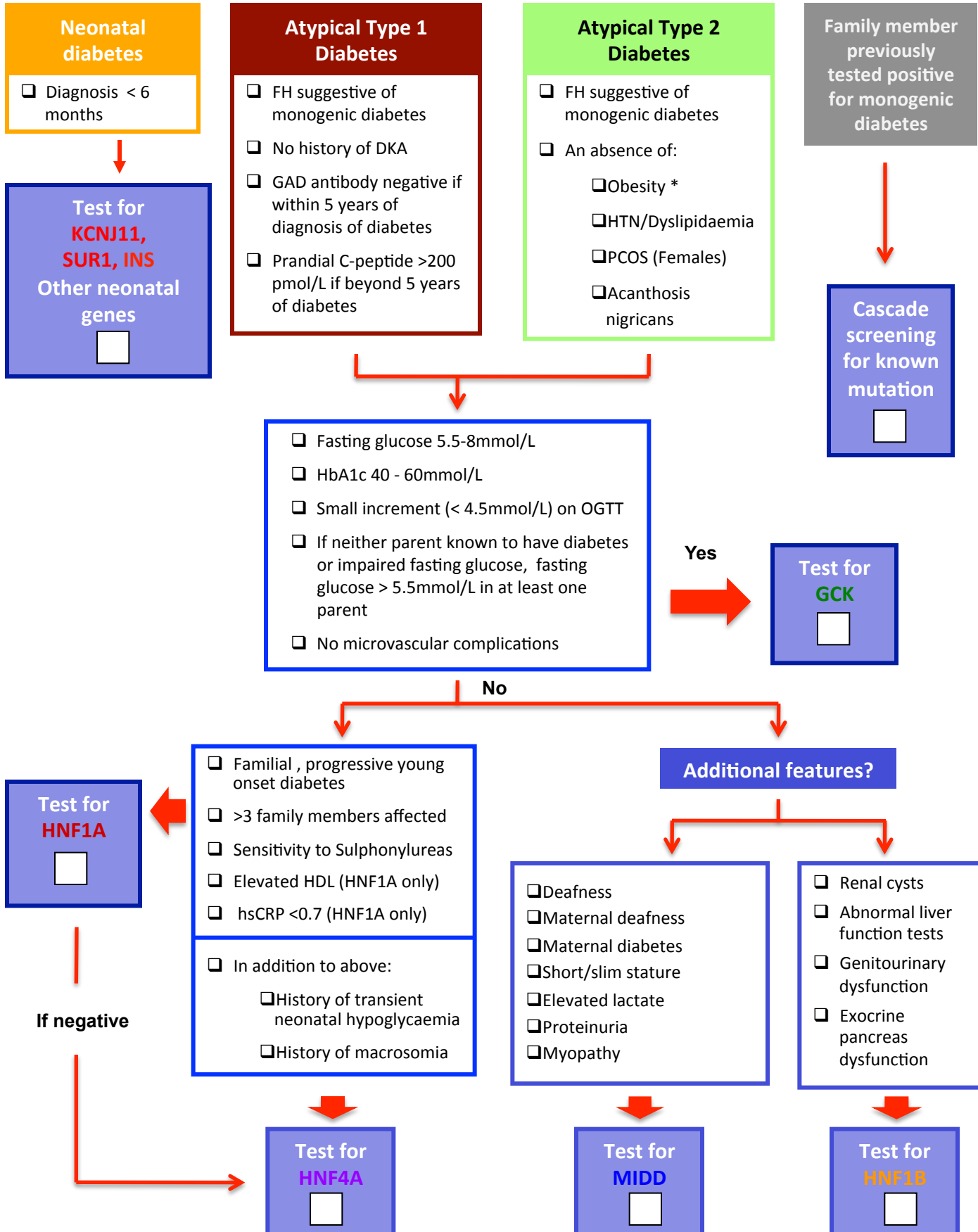
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Form A: Diagnostic algorithm for suspected monogenic diabetes (diabetes < 35 yrs)

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Please tick all that apply in algorithm along with requested genetic test



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Form B: Molecular genetics test form for monogenic diabetes

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SHIP TO: Molecular Genetics Laboratory,
LabPlus, Level 2,
Building 31, Auckland City
Hospital,
Grafton, Auckland,
New Zealand.
E-Mail: molgen@adhb.govt.nz
Tel: +64-9-3074949 x 6356
Fax: +64-9-307 2826

Molecular Genetics Test Request Form

Patient Details:		Date:					
Name (Surname, forename):		DOB (dd/mm/yy):	Gender:				
Ethnicity (Country of Origin):		Hospital (ref) number:					
Test requested:							
Clinical details:	Form A Attached	Cascade test	Yes / No				
Age at diabetes diagnosis:		History of DKA yes <input type="checkbox"/> no <input type="checkbox"/>					
Current diabetes treatment:							
Not currently on insulin <input type="checkbox"/> insulin within 6 months of diagnosis <input type="checkbox"/> insulin over 6 months after diagnosis <input type="checkbox"/>							
Height _____ Weight _____ BMI _____							
HbA1c: _____ Concurrent diabetes treatment: _____							
Parents affected with diabetes:		Mother	age at diagnosis of diabetes _____				
		Father	age at diagnosis of diabetes _____				
		<table border="1"><tr><td>Yes</td><td>No</td></tr><tr><td></td><td></td></tr></table>	Yes	No			
Yes	No						
Number of generations with diabetes:							
Additional information :							

Requesting Doctor

Name:	Tel:
E-mail:	Fax:
Signature:	
Address	Send additional copy of report to:

If billing is to be sent to other than the referring doctor, please provide appropriate information below

Institution/ Organisation:	
Address	Attn:
	Tel:
	Fax:
	Email
Sample type:	DNA conc:
Collection date:	Extraction method/date:
<i>For Lab Use:</i>	Lab ID:
Date received:	Vol DNA received:

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Form C: Patient information sheet for monogenic diabetes database

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PARTICIPANT INFORMATION SHEET

Monogenic diabetes Database

Purpose of the Study

You are invited to take part in a study because your doctor has advised you to have a test for monogenic diabetes (genetic diabetes). We would like to link this test result with some information about your diabetes or risk of diabetes and add this to a New Zealand monogenic diabetes database, held at Auckland University. The long term aim of this study is to better understand monogenic diabetes (diabetes caused by a single gene change) in New Zealand. The sort of questions we wish to answer are: Which diabetes related clues help identify people with certain monogenic diabetes best? How do these differ in those who were first picked up compared to those who were picked up because someone else in their family was known to have this?

Genetic tests for diabetes

You are being asked to take part in this study because your doctor has requested a test for genetic diabetes, as part of your routine care. We are asking people who have recently been asked to take a test for monogenic diabetes and also people who may have had a test done several years ago, to have their details collected in a database.

If my genetic test came back negative, am I still able to be included on the database? Yes, it does not matter whether you tested positive or negative for the diabetes genetic test. Your information is very important to help us decide how to improve the criteria for testing in future.

Why is getting the diabetes diagnosis right, so important? Your doctor will already have explained why they thought you should have a genetic test for diabetes, but in summary getting the diagnosis right may alter the diabetes treatment for you and/or your family. It may also be important for the management of women with a family history of genetic diabetes who are; a) pregnant or who are b) planning pregnancy.

What exactly am I consenting to, if I agree to have my clinical information added to the NZ monogenic diabetes database? We will ask your doctor to supply us with clinical information that is routinely collected when genetic tests for diabetes are arranged. This information will include date of birth, gender, age of onset of diabetes (if relevant), details of your family history of diabetes such as relationship to you and age of diagnosis (if known). It may sometimes include your birth weight and birth weight of family members and the type of diabetes treatments you or family members have received (where relevant). The database will also include blood test results, including the results of your genetic test.

How will information on the database be kept secret and who will have access to the database? The database has several levels of security and strict password access by only the three diabetes doctors involved in this study.

How will I know what information about me is on the database and how can I update it if more information about my family comes through? You may ask your referring health care professional for a copy of the referral information. If anything changes, you can submit this information directly to the principle investigator who specializes in monogenic diabetes, Dr Rinki Murphy using email: R.Murphy@auckland.ac.nz

Can I ask for my information to be removed from the database? How do I go about doing this? Yes, you can let Dr Rinki Murphy know using email: R.Murphy@auckland.ac.nz

Will the principle investigator and/or her team contact me directly at any stage? Usually we will contact your health care professional regarding any developments in monogenic diabetes that may affect your health care, but we may contact you directly if there are important issues to update you about.

How will the researchers know I've changed my GP or moved away? We will rely on the contact information about you that your doctor who referred you has, or any updated information you give us directly

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We hope that you find this project interesting, but you are under no obligation to take part. Options regarding your participation are outlined individually in the consent form. Please feel free to discuss this with your family, friends or family doctor.

Maori Ethics Committee Review Committee do not support tissue banking in any form given collective whanau, hapu, iwi implications. However they have noted individuals have the right to make their own decisions.

If you have any queries or concerns regarding your rights as a participant in this research study, you can contact an independent Health and Disability Advocate. This is a free service provided under the Health and Disability Commissioner Act:

Telephone (NZ wide): 0800 555 050
Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT)
Email: advocacy@hdc.org.nz

Principal Investigator: Dr Rinki Murphy
Department of Medicine
Faculty of Medical and Health Sciences
University of Auckland
Tel: 09 373 7599 ext 86313
R.Murphy@auckland.ac.nz

Study investigators:

Dr Helen Lunt Diabetes Centre Christchurch Hospital Private Bag 4710 , Christchurch Helen.Lunt@cdhb.govt.nz	Dr Richard Carroll Endocrine, Diabetes and Research Centre Wellington Regional Hospital Tel: 04 806 2140 richard.carroll@ccdhb.org.nz
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Form D: Adult consent form for NZ Monogenic diabetes database

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THE UNIVERSITY OF AUCKLAND
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WRITTEN CONSENT FORM FOR MONOGENIC DIABETES DATABASE

Title of project: New Zealand Monogenic Diabetes Database

Principal Investigator: Dr Rinki Murphy

Name of Patient: D.O.B.....

Ethnicity..... Sex: Male/Female

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Oute mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
	Other languages to be added following consultation with relevant communities.		

I, _____ have been given, and I have read, and I understand the information sheet dated 1 August 2012, version 1.0, for volunteers taking part in the study designed to establish a New Zealand Monogenic Diabetes Database. I have had the opportunity to discuss this study and I am satisfied with the answers I have been given.

YES/NO

I give consent to my personal details (including family tree), medical history and genetic analysis results to be stored electronically in the NZ Monogenic Diabetes Database

YES / NO

I give consent for the researchers to contact me about any new developments relating to my diabetes diagnosis or participation in research to find out more about this.

YES /NO

I agree to my GP or other current care provider being informed of my participation in this study / the results of my participation in this study.

YES/NO

Signed (Subject): Date

(Parent/Guardian) Date

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Form D continued: Adult consent form

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(Parent/Guardian) Date

In my opinion consent was given freely and with full understanding.

Witness name (please print):

Witness signature: Date

Consent obtained by:

Name (please print)

Signed: Date

This study has received ethical approval from the Northern A Health and Disability Ethics Committee
Reference 12/NTA/87

Dr Rinki Murphy
Department of Medicine
Faculty of Medical and Health Sciences
University of Auckland
Tel : 09 373 7599 ext. 86313
R.Murphy@auckland.ac.nz

Dr Richard Carroll
Endocrine, Diabetes and Research Centre
Wellington Regional Hospital
Tel: 04 806 2140
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Dr Helen Lunt
Diabetes Centre
Christchurch Hospital
Private Bag 4710
Christchurch
Helen.Lunt@cdhb.health.nz

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Form E: Child information sheet for monogenic diabetes database

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We were wondering if you would like to help us....



What will we do?

- Your doctor has already explained that you need a gene test to find out the cause of your diabetes
- We want to store the information about your diabetes and your gene test result in a secure computer
- From the stored information, we will be able to find out things about the different types of diabetes caused by genes and how best to treat these and find if other people also carry this gene.

Any details we have about you are *kept secret*, and nobody else will ever be able to get hold of any information about you or your genetic result.

If you *change your mind* in the future and don't want to take part, *that is OK*, and we will remove all your information from our study.

Will I need to give a blood sample?

NO - this study will only collect information about you and any tests your doctor has already done !

❖ The papers given to your parents/caregiver has even more stuff about this, so talk to them if you want to know more

❖ If you decide to help us the Doctor will talk to you to make sure that you understand everything and they will answer any questions

Why do we need your help?

- Lots of children and adults around the world develop a special type of diabetes that is quite rare and needs to be treated differently from the common types of diabetes. Finding out that diabetes is caused by a single gene disorder, can change the way your diabetes is treated.
- Sometimes if you were treated with insulin you may be able to be treated with tablets.
- Knowing who tested positive or not will help us get it right more often

If your parents say no and you don't take part in this study, it will make no difference to how you are looked after.

Thanks for thinking about it

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Form F: Child consent form for inclusion in monogenic diabetes registry

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HEALTH SCIENCES

CHILDREN'S CONSENT FORM FOR TAKING PART IN MONOGENIC DIABETES DATABASE

Title of project:

Monogenic diabetes database

Ihave read page 1 of this form and I have
had the study explained to me. Yes /No

I have had answers to the questions I asked, and know that I can ask
more questions at any time Yes /No

I agree to the study Doctors looking at my hospital notes
Yes/No

Signed (Subject): Date

Consent obtained by:
Name (please print)

Signed: Date