

Monogenic Diabetes (Including Maturity Onset Diabetes of the Young (MODY)) Panels

- I. Multigene panel analysis to establish or confirm a diagnosis of monogenic diabetes (including maturity-onset diabetes of the young (MODY)) is considered **medically necessary** when:
 - A. The member has a diagnosis of diabetes within the first 12 months of life, **OR**
 - B. The member has a diagnosis of diabetes before 30 years of age, **AND**
 1. The member has at least one of the following:
 - a) Autoantibody negative, **OR**
 - b) Retained C-peptide levels, **OR**
 - C. The member has a diagnosis of diabetes not characteristic of type 1 or type 2 diabetes, **AND**
 1. The member has a family history of diabetes consistent with an [autosomal dominant pattern of inheritance](#).
- II. Multigene panel analysis to establish or confirm a diagnosis of monogenic diabetes (maturity-onset diabetes of the young (MODY)) is considered **investigational** for all other indications.

RATIONALE AND REFERENCES

Monogenic Diabetes (Including Maturity Onset Diabetes of the Young (MODY)) Panels

American Diabetes Association

In 2024, the American Diabetes Association made the following recommendations (p. S32):

- Individuals of any age who were diagnosed with diabetes in the first 6 months of life should have immediate genetic testing for neonatal diabetes (Category A).
- Children and those diagnosed in early adulthood who have diabetes not characteristic of type 1 or type 2 diabetes that occurs in successive generations (suggestive of an autosomal dominant pattern of inheritance) should have genetic testing for maturity-onset diabetes of the young (Category A)

American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: standards of care in diabetes-2024. *Diabetes Care*. 2024;47(suppl 1):S20-S42. doi:10.2337/dc24-S002

Murphy, et al.

Murphy, et al. (2023) performed a systematic review and issued an expert opinion on how to use precision diagnostics to identify individuals with monogenic diabetes. The article states that the following individuals should be offered testing for monogenic diabetes:

1. All patients diagnosed with diabetes before the age of 6 months should be tested for monogenic forms of neonatal diabetes using the large-gene panel.
2. All patients diagnosed between 6 and 12 months should be tested for monogenic forms of neonatal diabetes using the large-gene panel. No demonstrable yield of monogenic etiology to support reflexive genetic testing patients diagnosed with diabetes between 12-24 months.
3. Women with gestational diabetes and fasting glucose above 5.5 mmol/L without obesity* should be tested for GCK etiology.
4. Those with persisting, mild hyperglycemia (HbA1c 38–62 mmol/mol, or fasting glucose 5.5–7.8 mmol/L) at any age, in the absence of obesity* should be tested for GCK etiology.
5. People without obesity under the age of 30 years who are either autoantibody negative and/or have retained C-peptide levels should be tested for monogenic diabetes using a large-gene panel (p.10).

Murphy R, Colclough K, Pollin TI, et al. The use of precision diagnostics for monogenic diabetes: a systematic review and expert opinion. *Commun Med (Lond)*. 2023;3(1):136. Published 2023 Oct 5. doi:10.1038/s43856-023-00369-8

International Society for Pediatric and Adolescent Diabetes (ISPAD)

In 2022, the International Society for Pediatric and Adolescent Diabetes (ISPAD) released a clinical practice consensus guideline for the diagnosis and management of monogenic diabetes in children and adolescents. The statement includes the following recommendations for genetic testing in the setting of neonatal diabetes and maturity onset diabetes of the young:

“All infants diagnosed with diabetes in the first 6 months of life are recommended to have immediate molecular genetic testing. Genetic testing may be considered in infants diagnosed between 6 and 12 months, especially in those without islet autoantibodies or who have other features suggestive of a monogenic cause” (p. 1190).

“The diagnosis of maturity onset diabetes of the young (MODY) is recommended in the following scenarios: family history of diabetes in a parent and first-degree relatives of that affected parent in persons with diabetes who lack the characteristics of T1D and T2D” (p. 1191).

Greeley SAW, Polak M, Njølstad PR, et al. ISPAD Clinical Practice Consensus Guidelines 2022: The diagnosis and management of monogenic diabetes in children and adolescents. *Pediatr Diabetes*. 2022;23(8):1188-1211. doi:10.1111/pedi.13426

DEFINITIONS

1. **Autosomal dominant pattern of inheritance** refers to a type of transmission of a genetic condition in which only one mutated copy of a gene (rather than two) is necessary for an individual to manifest the disease. These conditions are generally characterized by the following traits:
 - a. There are individuals with the condition in multiple generations of a family
 - b. Individuals who do not have the condition do not have children with the condition
 - c. Individuals with the condition have a parent with the condition