

**Supplementary Table 1: Search strategy using PubMed**

Question 1: Who should you test for monogenic diabetes	Number of References
Query	
<p><b>#1</b>            Diabetes Mellitus, Permanent Neonatal" [Supplementary Concept]) OR ( "Maturity-Onset Diabetes Of The Young, Type 9" [Supplementary Concept] OR "Maturity-Onset Diabetes of the Young, Type 7" [Supplementary Concept] OR "MODY, Type 6" [Supplementary Concept] OR "Maturity-Onset Diabetes of the Young, Type 8, with Exocrine Dysfunction" [Supplementary Concept] OR "Maturity-Onset Diabetes of the Young, Type 1" [Supplementary Concept] OR "Maturity-Onset Diabetes of the Young, Type 2" [Supplementary Concept] OR "Maturity-Onset Diabetes of the Young, Type 3" [Supplementary Concept] OR "Maturity-Onset Diabetes of the Young, Type 4" [Supplementary Concept] ) OR ( "Lipodystrophy, Congenital Generalized"[Mesh] OR "Diabetes Mellitus, Congenital Autoimmune" [Supplementary Concept] ) OR "Lipodystrophy"[Mesh] OR "Pancreatic Agenesis, Congenital" [Supplementary Concept] OR "Pancreatic Hypoplasia, Congenital, with Diabetes Mellitus and Congenital Heart Disease" [Supplementary Concept] OR "Donohue Syndrome"[Mesh] OR "Mason-Type Diabetes" [Supplementary Concept] OR "Lipodystrophy, Familial Partial"[Mesh] OR "Renal cysts and diabetes syndrome" [Supplementary Concept] OR ( "Diabetes Mellitus, Transient Neonatal, 2" [Supplementary Concept] OR "Diabetes Mellitus, Transient Neonatal, 3" [Supplementary Concept] OR "Diabetes Mellitus, Transient Neonatal, 1" [Supplementary Concept] OR "6q24-Related Transient Neonatal Diabetes Mellitus" [Supplementary Concept] ) OR "Noninsulin-dependent diabetes mellitus with deafness" [Supplementary Concept] Filters: English</p>	<p><b>4731</b></p>
<p><b>#2</b>            "monogenic diabetes"[Title/Abstract] OR "neonatal diabetes"[Title/Abstract] OR "maturity onset diabetes of the young"[Title/Abstract] OR "maturity-onset diabetes of the young"[Title/Abstract] OR "infancy onset diabetes"[Title/Abstract] OR "infancy-onset diabetes"[Title/Abstract] OR "congenital diabetes"[Title/Abstract] OR TNDM OR PNDM* OR "early onset diabetes"[Title/Abstract] OR "early-onset diabetes"[Title/Abstract] OR "syndromic diabetes"[Title/Abstract] OR lipodystroph* OR "mitochondrial diabetes"[Title/Abstract] OR "pancreatic agenesis"[Title/Abstract] OR "pancreatic hypoplasia"[Title/Abstract] OR leprechaun* OR "donohue syndrome"[Title/Abstract] OR "rabson mendenhall"[Title/Abstract] OR rabson-mendenhall OR dunnigan OR "wolfram syndrome"[Title/Abstract] OR RCAD OR "renal cysts and diabetes"[Title/Abstract] OR "chromosome 17q12 deletion syndrome"[Title/Abstract] OR "chromosome-17q12 deletion syndrome"[Title/Abstract] OR "mason type diabetes"[Title/Abstract] OR "mason-type diabetes"[Title/Abstract] OR "transient neonatal diabetes"[Title/Abstract] OR "permanent neonatal diabetes"[Title/Abstract] OR maternally inherited diabetes and deafness OR "M.3243A&gt;G mutation"[Title/Abstract] OR "mitochondrial tRNA"[Title/Abstract] OR "MODY" Filters: English</p>	<p><b>14256</b></p>
<p><b>#3</b>  <b>#1 OR #2</b></p>	<p><b>14295</b></p>

<b>#4</b> "Hepatocyte Nuclear Factor 1-beta"[Mesh] OR "Hepatocyte Nuclear Factor 1-alpha"[Mesh] OR "Hepatocyte Nuclear Factor 4"[Mesh] Filters: English	<b>3585</b>
<b>#5</b> HNF1A OR HNF1-A OR "hepatocyte nuclear factor 1"[Title/Abstract] OR "hepatocyte nuclear factor 1a"[Title/Abstract] OR "hepatocyte nuclear factor 1 alpha"[Title/Abstract] OR "HNF1 alpha"[Title/Abstract] OR HNF1alpha OR HNF4A OR HNF4-A OR HNF-4A OR "hepatocyte nuclear factor 4"[Title/Abstract] OR "hepatocyte nuclear factor 4a"[Title/Abstract] OR "hepatocyte nuclear factor 4 alpha"[Title/Abstract] OR HNF4alpha OR GCK OR HNF1B OR HNF1-b OR HNF-1B OR "hepatocyte nuclear factor 1b"[Title/Abstract] OR "hepatocyte nuclear factor 1 beta"[Title/Abstract] OR HNF1beta OR "HNF-1 beta"[Title/Abstract] OR "INS gene"[Title/Abstract] OR "INS mutation"[Title/Abstract] OR KCNJ11[Title/Abstract] OR ABCC8[Title/Abstract] OR PDX1[Title/Abstract] OR CEL-MODY [Title/Abstract] OR "CEL gene"[Title/Abstract] OR "CEL mutation"[Title/Abstract] OR "carboxyl ester lipase"[Title/Abstract] OR NEUROD1[Title/Abstract] OR WFS1[Title/Abstract]	<b>11142</b>
<b>#6</b> (INSR[Title/Abstract]) AND (diabetes[Title/Abstract]) Filters: English	<b>273</b>
<b>#7</b> (LMNA[Title/Abstract] OR PPARG[Title/Abstract] OR PLIN1[Title/Abstract]) AND (lipodystrophy[Title/Abstract]) Filters: English	<b>347</b>
<b>#8</b> #4 OR #5 OR #6 OR #7	<b>11988</b>
<b>#9</b> #3 OR #8	<b>23982</b>
<b>#10</b> "Diagnosis"[Mesh] Filters: English	<b>7662064</b>
<b>#11</b> "Phenotype"[Mesh] Filters:English	<b>307182</b>
<b>#12</b> Neonatal Screening[Mesh] Filters:English	<b>9677</b>
<b>#13</b> "etiology" [Subheading] Filters:English	<b>8144644</b>

<b>#14</b> Biomarkers[MeSH] Filters:English	<b>760545</b>
<b>#15</b> #10 OR #11 OR #12 OR #13 OR #14	<b>7868628</b>
<b>#16</b> diagnosis[Title/Abstract] Filters: English	<b>1367001</b>
<b>#17</b> "clinical characterist*" [Title/Abstract] Filters: English	<b>72805</b>
<b>#18</b> "identif*" [Title/Abstract] Filters:English	<b>3418989</b>
<b>#19</b> phenotyp* [Title/Abstract] Filters: English	<b>613305</b>
<b>#20</b> "risk score*" [Title/Abstract] Filters: English	<b>25785</b>
<b>#21</b> "screening pathway*" [Title/Abstract] Filters: English	<b>127</b>
<b>#22</b> etiolog* [Title/Abstract] Filters: English	<b>258874</b>
<b>#23</b> "systematic assessment" [Title/Abstract] Filters: English	<b>2720</b>
<b>#24</b> biomarker* [Title/Abstract] Filters: English	<b>320083</b>
<b>#25</b> "clinical suspicion" [Title/Abstract] Filters: English	<b>12335</b>
<b>#26</b> #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25	<b>5290922</b>

<b>#27</b> #15 OR #26	<b>7868578</b>
<b>#28</b> #9 AND #27	<b>7487</b>
<b>#29</b> #28 Filters: English, Humans	<b>6119</b>
1990-2000: 626 2001-2010: 2138 2011-2021: 3025	
<b>Question 2 How should you test someone for monogenic diabetes</b>	
<b>#30</b> (((("High-Throughput Nucleotide Sequencing"[Mesh]) OR "Whole Exome Sequencing"[Mesh]) OR "Multiplex Polymerase Chain Reaction"[Mesh]) OR "Real-Time Polymerase Chain Reaction"[Mesh]) OR "Chromatography, High Pressure Liquid"[Mesh]) OR "Polymorphism, Restriction Fragment Length"[Mesh] Filters: Humans, English	<b>156758</b>
<b>#31</b> "next generation sequencing"[Title/Abstract] OR "next-generation sequencing"[Title/Abstract] OR "sanger sequencing"[Title/Abstract] OR "dna sequencing"[Title/Abstract] OR "multigene panel"[Title/Abstract] OR "genetic testing"[Title/Abstract] OR "genetic screening"[Title/Abstract] OR "dna pooling"[Title/Abstract] OR "high-throughput sequencing"[Title/Abstract] OR "high throughput sequencing"[Title/Abstract] OR "targeted sequencing"[Title/Abstract] OR "target region capture sequencing"[Title/Abstract] OR "exome sequencing"[Title/Abstract] OR "genome sequencing"[Title/Abstract] OR mipa OR "dosage analysis"[Title/Abstract] OR "cnv detection"[Title/Abstract] OR "cnv analysis"[Title/Abstract] OR "allele specific pcr"[Title/Abstract] OR "real-time pcr"[Title/Abstract] OR "fluorescent pcr"[Title/Abstract] OR taqman OR sscp OR hplc OR rflp OR "chip n3 genotyping"[Title/Abstract] OR "whole exome sequencing"[Title/Abstract] OR "multiplex ligation dependent probe amplification"[Title/Abstract] OR "allele specific polymerase chain reaction"[Title/Abstract] OR "real time polymerase chain reaction"[Title/Abstract] OR "single strand conformation polymorphism"[Title/Abstract] OR "high performance liquid chromatography"[Title/Abstract] OR "restriction fragment length polymorphism"[Title/Abstract] Filters: Humans, English =304221	<b>304221</b>
<b>#32</b> #30 OR #31	<b>335251</b>
<b>#33</b> #9 AND #32	<b>1460</b>

Paper per decade	1990-2000: 114 2001-2010: 301 2011-2021: 1041
<b>Question 6 What are the next steps after a diagnosis of monogenic diabetes</b>	
#91 ("Genetic Counseling"[Mesh]) OR "Cell-Free Nucleic Acids"[Mesh] Filters: Humans, English	16553
#92 "cascade testing"[Title/Abstract] OR "cascade screening"[Title/Abstract] OR "genetic counselling"[Title/Abstract] OR "cell-free dna"[Title/Abstract] OR "cell free dna"[Title/Abstract] OR "noninvasive prenatal testing"[Title/Abstract] OR "non-invasive prenatal testing"[Title/Abstract] Filters: Humans, English	<b>8338</b>
#93 #91 OR #92	21814
#94 #9 AND #93	<b>61</b>
#95 "Penetrance"[Mesh] OR "Oceanic Ancestry Group"[Mesh] OR "American Native Continental Ancestry Group"[Mesh] OR "Asian Continental Ancestry Group"[Mesh] OR "European Continental Ancestry Group"[Mesh] OR "African Continental Ancestry Group"[Mesh] OR "Economic evaluation"[Mesh] OR "Continental Population Groups"[Mesh] Filters: Humans, English	<b>223571</b>
#96 variant[Title/Abstract] AND (unknown[Title/Abstract] OR significan*[Title/Abstract] OR ancestry group[Title/Abstract] OR penetrance[Title/Abstract] OR economic evaluation[Title/Abstract]) Filters: Humans, English	<b>4866</b>
#97 #95 OR #96	<b>2601031</b>
#98 #9 AND #97	<b>844</b>
<i>Papers per decade</i>	<i>1990-2000: 87 2001-2010: 308 2011-2020: 492</i>
<b>Question 7 What are the current challenges for the field in precision diagnostics?</b>	
#26 'variant'/exp OR 'ancestry group'/exp OR 'penetrance'/exp OR 'economic evaluation'/exp	992252
#27 ( 'variant of unknown significance':ab,ti OR 'variant n3':ab,ti) AND (unknown:ab,ti OR significan*:ab,ti) OR 'ancestry group':ab,ti OR penetrance:ab,ti OR 'economic evaluation':ab,ti	33291

#28 #26 OR #27	992252
Combined Search #35 #7 AND #28 2230 records AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) 1004 records Filter Human, English 859 records NOT 'conference abstract':it	<b>201</b>
<i>Papers per decade</i>	1990-2000: 4 2001-2010: 32 2011-2020:165

**Supplementary Table 2 PICOTS**

	<b>Diagnostic validity</b>
<b>Population</b>	Patients with diabetes
<b>Intervention</b>	Genetic testing for monogenic diabetes (using at least sequencing of a single gene if not multiple genes or whole exome or whole genome)
<b>Comparison</b>	Unselected vs selected cases using various clinical or biomarker criteria to increase yield of monogenic diabetes
<b>Outcomes</b>	<ul style="list-style-type: none"><li>· Diagnostic yield (fraction and percentage)</li><li>· Sensitivity/specificity (if thresholded)</li><li>· AUROC (if not thresholded)</li><li>· PPV/NPV</li></ul>
<b>Timing</b>	n/a
<b>Setting</b>	n/a

**Supplementary Table 3: Complete set of papers extracted for question 1. Who to test for monogenic diabetes.**

Study Details	Study type, Country, Ancestry of Participants	n=Number of probands, M:F Males:Females BMI	Method and genes tested	Variant curation method	Characteristics of diabetes population tested (age of diagnosis, or other clinical or biomarker criteria)	Individuals diagnosed, yield by different selection approaches
<b>Neonatal Diabetes</b>						
DeFranco (2015) [1]	Cohort study, International, referred to Exeter Molecular Genetics from 79 countries	n=1021 neonates with NDM, M:F 571:449, BMI NA	Type of genetic testing: Neonatal Diabetes Panel. Genes Sequenced: 6q24, ABCC8, EIF2AK3, FOXP3, GATA4, GATA6, GCK, GLIS3, HNF1B, IER3IP1, INS, KCNJ11, IER3IP1, MNX1, NEUROD1, NEUROG3, NKX2-2, PDX1, PTF1A, RFX6, SLC2A2, SLC19A2, ZFP57	Bioinformatics method ALAMUT	Diagnosed with diabetes before 6 months of age	Overall Yield 840/1021 (82%) including 30 GCK, 1 HNF1B, 150 ABCC8, 240 KCNJ11, 110 INS, 1 RFX6, 3 NEUROD1, 6 PDX1, 76 EIF2AK3, 22 PTF1A, 14 FOXP3, 113 6q24, 7 SLC19A2, 29 GATA6, 4 GATA4, 9 GLIS3, 1 IER3IP1, 1 MNX1, 1 NEUROG3, 2 NKX2-2, 6 SLC2A2, 12 ZFP57
Besser (2016) [2]	Cohort study, United Kingdom,	n=750, M:F 333:417, BMI NA	Type of genetic testing: Neonatal diabetes panel. Genes sequenced: GCK; HNF1B; KCNJ11, ABCC8, INS (all patients). 6q24, EIF2AK3, NEUROD1, RFX6, GCK, FOXP3, SLC19A2, GLIS3, PDX1, PTF1A, NEUROG3, HNF1B, BSCL2 (if clinically indicated).	Local lab guidelines	Patients with neonatal diabetes (hyperglycemia presenting <26 weeks of age) who were referred for genetic testing and who had a gestational age provided.	Neonatal DM (diabetes diagnosed <26 weeks): 598/750 (79.7%); -Preterm (<37 wk) with neonatal DM: 66% (97/146); -Term (>=37 wk) with neonatal DM: 83% (501/604); -Very preterm (<32 wk) with neonatal DM: 31% (13/42)
Habeb (2012) [3]	Cross sectional study, United Kingdom, Arab and British	n=165, M:F Arab 60:28; British 39:38, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: KCNJ11, ABCC8, INS (all), EIF2AK3, GCK, FOXP3, GLIS3, SLC19A2, PTF1A, NEUROD1, RFX6, SLC2A2 (based on phenotype)	None specified	88 Arab and 77 British probands with neonatal diabetes	Arab group: 56/88; British group: 32/77



Gopi (2021) [4]	Cohort study, India, South East Asian - Indian	n=181, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: ABCC8, KCNJ11	ACMG	Neonatal diabetes diagnosed up to 6 months	Diabetes diagnosed before 6 months: 39/181
Edghill (2008) [5]	Cohort study, United Kingdom, Multiple ethnicities - international cohort	n=1044, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: INS	Local lab guidelines	Neonatal diabetes diagnosed up to 2 years and young adults diagnosed up to 25 years from the Barts and Oxford (BOX) study and the British Diabetes Association 1972–1981 cohort.	<6 months, insulin treated, KCNJ11 negative: 35/285 -ND diagnosed <6 months yield: 33/141 -ND diagnosed 6-12 months yield: 2/86 -ND diagnosed >12 months yield: 0/58 -MODY yield in probands with clinically diagnosed MODY: 1/296 -Mutation rate found in type 2 diabetes diagnosed<45: 1/463
DeFranco (2013) [6]	Cross sectional study, United Kingdom, Multiple ethnicities - international cohort	n=103, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: PDX1	None specified	Probands with permanent neonatal diabetes diagnosed before 6 months	Diabetes <6 months, mutations in ABCC8, KCNJ11 and INS (and EIF2AK3 in consanguineous) had been excluded, None of the patients had pancreatic agenesis or exocrine insufficiency: 3/103
Shaw-Smith (2012) [7]	Cohort study, United Kingdom, Multiple ethnicities - internationally cohort	n=212, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: SLC19A2	None specified	International probands with permanent neonatal diabetes diagnosed up to 6 months	Total yield index (dx <6 months) and extended (dx>6 months): 5/400 -ND diagnosed <6 months of unknown genetic cause: 3/212; -ND diagnosed >6 months: 2/188
Borowiec (2012) [8]	Cross sectional study, Poland, Polish	n=211, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	None specified	Either diabetes diagnosed before 6 months or 2 or more clinical criteria of MODY diagnosed up to 35 years	Neonatal Diabetes and negative KCNJ11, ABCC8, INS: 1/17 homozygous GCK; >2 MODY criteria: 68/194; Negative for GCK: 0/126

Rubio-Cabezas (2012) [9]	Cross sectional study, Spain,	n=520, M:F NA, BMI NA	Type of genetic testing: Neonatal diabetes panel. Genes sequenced: GCK, KCNJ11, INS, ABCC8	None specified	Infants with diabetes diagnosed < 12 months old	Total age 0-52 weeks: 272/550 (49.5%); KCNJ11: 144/550 (26%); ABCC8: 56/520 (11%); INS: 64/550 (12%); GCK 8/58 (screened after the others if no findings) -ND diagnosed <6 months yield: 263/405 -ND diagnosed 6-12 months yield: 9/145
Busiah (2013) [10]	Cohort study, France, Multiple Ethnicities, 20 countries	n=174, M:F NA, BMI NA	Type of genetic testing: Neonatal diabetes panel. Genes sequenced: 6q24, INS, KCNJ11, ABCC8	None specified	French Neonatal Diabetes Study Group - neonatal diabetes diagnosed up to 12 months	All unrelated cohort participants: 127/174; -6q24: 40/174; KATP (KCNJ11/ABCC8): 74/174; INS: 13/174 -ND diagnosed <6 months yield among all diagnosed <12m: 64/155 -ND diagnosed 6-12 months yield among all diagnosed <12m: 5/18
Gopi (2021) [11]	Cohort study, India, South East Asian - Indian	n=189, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: INS	ACMG	Antibody negative children with neonatal diabetes diagnosed up to 9 months from India.	<9 months, persists >12 months of age, antibody negative, C-peptide detectable: 8/189 -ND diagnosed <6 months of total group diagnosed <9 months: 8/189 -ND diagnosed 6-9 months of total group diagnosed <9 months: 0/189
Flanagan (2006) [12]	Cross sectional study, United Kingdom, Multiple ethnicities - international cohort	n=239, M:F 129:110, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: KCNJ11	None specified	Permanent diabetes diagnosed before 2 years of age	Total cohort ND yield: 31/239 -ND diagnosed <6 months: 31/120 -ND diagnosed 6-12 months: 0/50 -ND diagnosed 12-24 months: 0/70

Edghill (2006) [13]	Case control study, United Kingdom, Multiple ethnicities - international cohort	n=187, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: KCNJ11	None specified	Recruited worldwide with diabetes diagnosed before 2 years of age	Permanent diabetes diagnosed under the age of 2 years: 32/187; -ND diagnosed <6 months: 32/79 -ND diagnosed 6-12 months: 0/45 -ND diagnosed 12-24 months: 0/63 -KCNJ11 positive, diagnosed with diabetes under the age of 6 months (n=32): 3% had highest risk HLA genotype, 16% protective genotypes, similar to healthy controls (3% and 17%); -KCNJ11 negative, diagnosed with diabetes <6months (n=47): 9% had highest HLA genotype, 17% protective genotypes
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**Gestational Diabetes: European Ancestry Predominant**

Chakera (2014) [14]	Cohort study, UK and Ireland, 93% White European	n=356, M:F 0:400, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	Local lab guidelines	Atlantic Diabetes in Pregnancy (Atlantic DIP) cohort in which all women with GDM, and a random group without GDM, had GCK sequencing. Characteristics of women diagnosed with GCK-MODY during pregnancy were also analyzed.	Yield of GCK cases per total with genetic testing: 4/356 -GDM with fasting glucose <5.1 mmol/L: 0/109 -GDM with fasting glucose 5.1-5.5 mmol/L: 1/129 -GDM with fasting glucose >=5.5 mmol/L: 3/118
Gjesing (2017) [15]	Cohort study, Denmark, Danish	n=354, M:F 0:354, BMI 27.6 (23.9-32.9)	Type of genetic testing: Large MODY panel (>= 5 genes). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; INS	ACMG	Antibody negative women with diet-treated GDM recruited in Denmark	Diet-treated GDM: 21/354
Zubkova (2019) [16]	Cohort study, Russia, Russian	n=188, M:F 0:188, BMI NA	Type of genetic testing: Large MODY panel (>= 5 genes). Genes sequenced: 28 gene panel	ACMG	Russian pregnant non-obese women with diabetes during pregnancy	GDM, non-obese: 59/188

**Gestational diabetes: Non-European**

Jiang (2022) [17]	Case control study, China, China, Shanghai	n=835 including 400 controls, M:F 229: 208 , BMI GDM: 22.7±3.4, GCK-MODY: 20.2±2.1)	Type of genetic testing: Single gene(s). Genes sequenced: GCK	GnomADFunctional studies	Women with GDM and controls	GDM: 15/411; Affected Fathers: 6/24; Health Controls: 0/400
<b>GCK: European Ancestry predominant</b>						
Valentínová (2012) [18]	Cohort study, Slovakia,	n=100, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	None specified	Individuals diagnosed up to age 35 years with a suspected diagnosis of GCK-MODY	Persistent and stable fasting hyperglycemia (5.5–10.0 mmol/L), HbA1c <8% [64 mmol/ml], age of diagnosis <35years, and when on insulin treatment, dose <0.4 IU/Kg/day: 36/100
Sagen (2008) [19]	Cohort study, Norway, Northern European	n=112, M:F NA, BMI GCK 22.3(+/-5.0) No GCK mutation 25.1(+/-4.7)	Type of genetic testing: Single gene(s). Genes sequenced: GCK	HGDM	Cases suspected to have MODY diagnosed up to 25 years referred to a diagnostic centre	Suspected MODY (initial referral): 23/329; Suspected MODY sequenced for GCK: 23/112
Pinelli (2013) [20]	Cohort study, Italy, Italian	n=232, M:F NA, BMI BMI Z-score close to zero	Type of genetic testing: Single gene(s). Genes sequenced: GCK	None specified	Used known GCK-MODY cases to devise diagnostic criteria composed of seven clinical, biochemical and anamnestic criteria for case finding of GCK-MODY prospectively in those aged 6 months-25 years.	Validated criteria in two retrospective cohorts and applied to prospective cohort of 921 patients of which 21 fulfilled 7 criteria and were tested with yield of 13/21.
Massa (2001) [21]	Cohort study, Italy, Italian	n=131, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	Local lab guidelines	Children with suspected GCK-MODY based on negative islet antibodies, family history and stable fasting hyperglycaemia	MODY pedigree index patients: 54/132; Chronic fasting hyperglycaemia, negative for serological markers of Type I (insulin-dependent) diabetes

						mellitus and glucose-tolerant parents: 3/9
Borowiec (2012) [22]	Intervention (campaign on MODY)., Poland, Polish	n=178, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	Checked against Human Gene Mutation Database	Cases referred with clinical suspicion of GCK-MODY following a public information campaign.	Yield 54/178 (30%)
Aykut (2018) [23]	Cohort study, Turkey, Turkish	n=177, M:F 85:92, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	Local lab guidelines	Clinically suspected MODY referred from 2009-2015. Diabetes diagnosed up to 50 years with a family history of diabetes and absence of islet autoantibodies.	Yield 79/177 (45%)
Aloi (2017) [24]	Cohort study, Italy, Italian	n=100, M:F 56:44, BMI Non-obese	Type of genetic testing: Single gene(s). Genes sequenced: GCK	Local lab guidelines	Impaired fasting glycaemia diagnosed 6 months to 56 years recruited from a single clinic 2009-2015. Group 1 "strict criteria": age of onset <25 yrs, FPG >99mg/dl, OGTT 2 hr 140mg/dl, absence of islet antibodies, family history, absence of obesity and no treatment. Group 2: IFG and absence of islet antibodies + at least one other MODY criteria.	Group 1 32 cases out of 36 (88%) Group 2 21 cases out of 64 (32%) Overall yield 53%

Lukášová (2008) [25]	Case control study, Czech Republic, Czech	n=722, M:F 210:490, BMI T2D: 30.53 +/- 5.53, GDM: 26.41 +/-5.03, Healthy offspring of DM: 25.51 + 4.16, Controls: 23.13 +/- 3.38	Type of genetic testing: Single gene(s). Genes sequenced: GCK	None specified	Clinically suspected MODY in cases of T2D, GDM and non-diabetic, with and without family history of diabetes	12 MODY probands: 2/12; GDM, T2D, offspring, controls: 0/710
Pace (2022) [26]	Cohort study, Malta, Maltese	n=145, M:F 59:86, BMI IFG: Median 27.6/IQR2.5, Diabetes:Median28.5/IQR 2.5	Type of genetic testing: Single gene(s). Genes sequenced: GCK	ACMG	Adults with suspected MODY diagnosed up to age 40 years from a single centre between 2018-2019.	All (IFG + Diabetes): 3/145; -Subgroup (IFG): 3/104
Vits (2006) [27]	Cohort study, Belgium, North European	n=124, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	Local lab guidelines	124 families, referred to a tertiary centre between 2002 and2005. All probands fulfilled at least two of the following criteria: early-onset hyperglycaemia (age of onset up to 40 years), the absence of islet autoantibodies and a positive familial history for diabetes	Hyperglycemia age < 40, autoantibody negative, positive family history with at least 2 generations affected: 33/124
Thomson (2003) [28]	Cohort study, United Kingdom,	n=212, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	Local lab guidelines	Suspected MODY, recruited for research or diagnostic referral	Research testing 29/86 (34%); Diagnostic testing 32/126 (25%)
<b>GCK: Non-European</b>						

Ma (2019) [29]	Cohort study, Other: China, Chinese	n=679, M:F NA, BMI NA	Type of genetic testing: Genes sequenced: GCK	ACMG	pre-diabetes, newly diagnosed diabetes and existing diabetes	GCK-MODY in Discovery cohort 11/545 (2%), Replication cohort 3/134 (2%), Test cohort using criteria fasting glucose 5.4-8.3 and TG<1.43: 1/207 (0.5%)
Carmody (2016) [30]	Cohort study, United States, Multiple ethnicities	n=135, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: GCK	Local lab guidelines	Proband from the US Monogenic Diabetes Registry with GCK-MODY phenotype had sequencing. Additional individuals with known GCK-MODY were also included in the study	Initial Criteria as follows: Chronic mild fasting hyperglycemia (100–140 mg/dl, 5.55–7.75 mmol/l) and HbA1c 5.6–7.8 % (38–62 mmol/mol) plus either a linear three-generation family history of hyperglycemia or diabetes mellitus or BMI less than 30 kg/m <sup>2</sup> in adults and BMI below the 95th percentile in children and age at diagnosis less than 30 years: 64/117; Initial criteria + negative autoantibodies: 3/7; Initial criteria + Latin ancestry: 4/8; Initial Criteria + Asian ancestry: 4/9
<b>Monogenic diabetes: European ancestry predominant</b>						
Ivanoshchuk (2021) [31]	Cohort study, Russian, Western Siberia	n=178, M:F NA, BMI NA	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: HNF4A,GCK,HNF1A,PDX1,HNF1B,NEUROD1,KLF11,CEL,PAX4,INS,BLK,KCNJ11,ABC8,APPL1	ACMG	Proband with diabetes diagnosed up to 35 years and clinically suspected MODY	<35 years, family history of diabetes, without obesity, islet autoantibody negative, normal or mildly reduced c-peptide, no insulin therapy, absence of diabetic ketoacidosis: 38/178
Saint-Martin (2022) [32]	Cross sectional study, France, Eurocaucasian	n=1676, M:F 771:905, BMI 23.5[20.5-27.2]	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: 18 gene panel	Monogenic Diabetes Expert Panel (ClinVar) rules, adapted from the ACMG guidelines	Proband referred for MODY genetic testing in France	Proband referred for MODY testing between 2017 and 2020: 307/1676

Colclough (2022) [33]	Cohort study, United Kingdom, Multiple ethnicity	n=1280, M:F 556:724, BMI 25.7(22.4–30.0)	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; LMNA; ABCC8, CEL, CISD2, GATA4, GATA6, INS, INSR, KCNJ11, MTTL1 m.3243A>G, NEUROD1, PAX6, PCBD1, PDX1, PLIN1, POLD1, PPARG, RFX6, SLC29A3, TRMT10A, WFS1, ZBTB20, ZFP57	ACMG	All referrals from U.K. clinicians for routine MODY genetic testing 2011-2018	Suspected MODY 297/1280; -MODY confirmed cases who had syndromic gene: 56/297; m.324A>G 24/56, HNF1B 18/56, 6 other genes (WFS1, INSR, GATA6, SLC29A3, TRMT10A, PPARG) 14/56 -Patients with syndromic variant with clinical features of syndrome without diabetes: 11/56
Shields (2017) [34]	Cross sectional study, United Kingdom, Multiple ethnicity (98% white)	n=216, M:F NA, BMI NA	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; LMNA; Mitochondrial genome	None specified	People with diabetes diagnosed <30 years of age, currently younger than 50 years, in two U.K. regions with existing high detection of monogenic diabetes (UNITED study).	UCPCR positive or Non-insulin treated with negative autoantibodies for IA2 and GAD: 51/216
Karaoglan (2021) [35]	Cross sectional study, Turkey, Turkish	n=230, M:F 113:117, BMI NA	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; LMNA; ABCC8, GATA6, INS, KCNJ11, NEUROD1, PAX6, PDX1, PPARG, INSR	None specified	Diagnosed up to 18 years with atypical presentation for type 1 and type 2 diabetes	Full cohort with MODY genetic variant: 24/230 including GCK (15), HNF1A (1), HNF4A (7), PDX1(1); -Lower total daily insulin dose: 20 MODY genetic variant/122; -Positive islet antibody: 4 MODY genetic variant/24



Bjørkhaug (2003) [36]	Cohort study, Norway, Norwegian	n=130, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A	Local lab guidelines	Families recruited from the Norwegian MODY Registry with either clinical MODY (fulfilled strict criteria including autosomal dominant inheritance in two generations, at least two relatives of the proband having either diabetes or impaired glucose tolerance, onset of diabetes before 25 yr of age in at least one subject, and reduced insulin secretion), suspected MODY (provider suspicion, limited clinical data), or pedigrees with multiplex type 1 diabetes.	Clinical MODY 22/42 (52%); Suspected MODY 15/75 (20%), Multiplex T1D 1/13 (7.7%)
Søvik (2013) [37]	Cross sectional study, Norway, Norwegian	n=not supplied, registry contains 198 families with MODY , M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A,GCK,HNF4A,HNF1B, CEL, INS, KCNJ11, ABCC8, NEUROD1	None specified	The Norwegian MODY registry, diagnosed up to 40 years	1500 tested referred cases: 458/1500; HNF1A (208/105 families)/ GCK (138/59 families); HNF4A (40/15 families)/HNF4B (19/11 families)/CEL (39/2 families), INS (9/4 families), NEUROD1 (4/2 families)
Frayling (2001) [38]	Cross sectional study, United Kingdom, 97% UK Caucasian	n=210, M:F , BMI NA	Type of genetic testing: Large MODY panel (>= 5 genes). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; IPF-1, NEUROD1	None specified	Type 2 diabetes diagnosed up to age 35 with clinical suspicion of MODY (specific MODY criteria fulfilled)	Full cohort (screened for frameshift mutation p.291fsinsC/p.291fsdelC): 24/210; MODY panel screening 101 sequenced: HNF1A 34, GCK 22, HNF4A 2, HNF1B 4

Johansson (2017) [39]	Case control study, Norway, European	n=938, M:F 554:384, BMI NA	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: HNF1A,GCK,HNF4A,HNF1B, INS,ABCC8,KCNJ11,BLK,CEL,NEUROD1,KLF11,PAX4,PDX1.	Score system as defined by Plon et al Hum Mut 2018	Norwegian Childhood Diabetes Registry diagnosed up to age 15, absence of islet antibodies. Genetic testing reported with and without class 3 variants (VUS)	Diabetes <15 years, antibody negative, class 3-5 variants: 30/462; Diabetes <15 years, antibody positive, class 3-5 variants: 11/468; Diabetes <15 years, antibody negative, class 4-5 variants: 19/462; Diabetes <15 years, antibody positive, class 4-5 variants: 1/468.
Donath (2019) [40]	Cross sectional study, France, 60% Eurocaucasian	n=1564, M:F 737:827, BMI NA	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: GCK,HNF1A,HNF4A,HNF1B, ABCC8,KCNJ11,INS	ACMG	Clinically suspected MODY from 116 Endocrinology departments, Islet antibody negative	At least 2 of a) age of onset 15-40 years; b) BMI < 30 kg/m <sup>2</sup> and c) at least 2 gen FH: 254/1564 (16%); Age of onset 15-40 years AND BMI < 30 kg/m <sup>2</sup> and AND at least 2 gen FH: 198/999 (20%); Age of onset 15-40 years AND BMI < 30 kg/m <sup>2</sup> and AND at least 2 gen FH AND EuroCaucasian origin: 54/504 (11%); At least 2 gen FH, age at onset $\leq 40$ years, and BMI < 25 kg/m: 101/301 (34%)

Bansal (2017) [41]	Case control study, Germany, Northern European	n=6888, M:F Stage 1 Cases: 1042:838 Stage 2 Cases: 1333:803 Stage 1 Controls: 852:988 Stage 2 Controls: NA, BMI Stage1 Cases:27.3 Stage2 Cases: 27.8 Stage1 Controls:25.6 Stage2Controls: 26.6	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: HNF1A,HNF4A,HNF1B,INS, NEUROD1,PDX1,PAX4,ABC C8,KCNJ11,KLF11,CEL,BLK, WFS1,NEUROG3,EIF2AK3, GLIS3,RFX6,SLC19A2,PAX, GATA6, PPARG	ACMG	Islet antibody negative with no clinical features of T1D recruited at tertiary centre. Not selected for typical MODY features and mean age $>40$ years.	Young onset and late onset type 2 diabetes: 47/4016; Young onset ( $<40$ ) diabetes: 29/1346; Older onset ( $\geq 40$ ) diabetes: 18/2670 (all the yields are for GCK, HNF1A, HNF4A, HNF1B, ABCC8 only)
Ateş (2021) [42]	Cohort study, Turkey, Turkish	n=182, M:F 94:88, BMI	Type of genetic testing: Large MODY panel ( $\geq 5$ genes). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; KCNJ11, ABCC8, INS	ACMG	Clinical diagnosis of MODY, diabetes diagnosed below 35, and family history of diabetes.	Clinical diagnosis of MODY diagnosed with diabetes before the age of 35: 30/182
Bennett (2015) [43]	Cohort study, United States, North America	n=184, M:F 47:53, BMI NA	Type of genetic testing: Single gene(s) (specify below). Genes sequenced: HNF1A; GCK; HNF4A; Other: INS, ABCC8, KCNJ11	Local lab guidelines	Patients with neonatal diabetes or diabetes suspected to be MODY referred to reference diagnostic laboratory	Neonatal diabetes or suspected MODY: 51/184 Subset number of ND vs MODY NA (1/3 of population had no phenotype data)

Irgens (2013) [44]	Cross sectional study, Norway, Norwegian	n=118, M:F NA, BMI NA	Type of genetic testing: Small MODY panel (<5 genes): KCNJ11, ABCC7, INS (PNDM); HNF1A; HNF4A, INS, MT3243A>G (MODY A); or GCK (MODY B).	None specified	Norwegian Paediatric diabetes Registry, diagnosed aged 0-14 years, includes 91% of children with diabetes.	PNDM Group: 4/24 (all KCNJ11, diagnosed <6m); MODY A (Autoantibody - and diabetes in parent): 6/46 (5 HNF1A, 1 INS) MODY B (A1c <7.4%, no insulin): 4/98 (3 GCK, 1HNF1A) Total estimated Norwegian prevalence (plus 30 extra from MODY registry): 48/323 autoantibody negative and patients not found in the NCDR registry of Norwegian children (15 patients)
Stankute (2020) [45]	Cross sectional study, Lithuania, Lithuanian	n=153, M:F 80:73, BMI NA	Type of genetic testing: Large MODY panel. Genes sequenced: 307 gene panel including 14 MODY and 28 NDM genes	None specified	LithuanianSwiss project, Lithuanian pediatric diabetes registry with absence of islet autoantibodies.	Yield 42/153 (27%)
Vaxillaire (2021) [46]	Cross sectional study, France , Multiple ethnicities	n=204, M:F 91:54, BMI NA	Type of genetic testing: Large MODY panel. Genes sequenced: 35 gene panel	ACMG	Unrelated individuals from 11 Mediterranean countries with a clinical suspicion of MODY	Overall yield 36/204 (17.6%)
Schober (2009) [47]	Cross sectional study, Germany and Austria,	n=272, M:F NA, BMI NA	Type of genetic testing: Small MODY panel (<5 genes). Genes sequenced: HNF1A; GCK; HNF4A	None specified	Diagnosed up to 18 years, clinically defined as MODY, based on family history and clinical presentation. 272 had diagnostic genetic testing through routine labs.	263/272 (97%) confirmed as MODY.
Misra (2016) [48]	Cohort study, United Kingdom, South Asian and European	n=4010, M:F NA, BMI NA	Type of genetic testing: Small MODY panel (<5 genes). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B	According to Wallis, et al, 2013. ACGS Practice guidelines	People referred for MODY testing at National centre whose ancestry was known	Individuals referred for MODY testing: 1011/3472; South Asian individuals referred for MODY testing: 37/293

Carlsson (2020) [49]	Cohort study, Sweden, Swedish	n=485, M:F 2178:1755, BMI Z score - 0.35 (1.55)	Type of genetic testing: Small MODY panel (<5 genes). Genes sequenced: HNF1A; GCK; HNF4A	ACMG	Paediatric probands newly diagnosed with diabetes between 2005-2010 for who there was an islet antibody result	Diagnosis 1-18 yrs, antibody negative x4: 46/303; Diagnosis 1-18 yrs, antibody positive: 0/182; Diagnosis 1-18 yrs, antibody negative, HbA1c <7.5% at dx or family history: 44/131; Diagnosis 1-18 yrs, antibody negative, positive family history: 29/96
Stanik (2014) [50]	Cohort study, Slovakia, Slovakian and Czech	n=150, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A; GCK; HNF4A	None specified	Probands diagnosed up to age 25 clinically suspected to be MODY but without family history of diabetes.	Patients fulfilling inclusion criteria: Total 85/150 including GCK 59, HNF1A 13, HNF4A 1
Bellanné-Chantelot (2016) [51]	Case control study, France, French	n=453, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A	None specified	Diagnosed up to 40 years, islet antibody absent with (1) Suspected HNF1A-MODY, (2) Familial young T2D (YT2D) (3) General T2D. Clinical model and use of hsCRP tested	Clinical model: HNF1A vs T2D, ROC C-statistic 0.99; HNF1A vs YT2D ROC C-statistic 0.82 Clinical model + CRP, HNF1A vs T2D ROC C-statistic 0.99, HNF1A vs YT2D ROC C-statistic 0.85
Pihoker (2013) [52]	Cross sectional study, United States, 36% Non-Hispanic white, 20 % African American, 31%hispanic, 11 % Asian/Pacific Islander	n=586, M:F 239:347, BMI NA	Type of genetic testing: Sanger sequencing. Genes sequenced: HNF1A; GCK; HNF4A	Local lab guidelines	Diabetes <20 yrs from the SEARCH study	All MODY 47/586 (8% of auto-antibody negative, C-peptide positive)

Lehto (1999) [53]	Cohort study, Sweden, Swedish, Finnish	n=115, M:F 55:60, BMI 26.5 (5.5)	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A; GCK; HNF4A; Mitochondrial genome	Local lab guidelines	Families with early-onset diabetes (up to age 40) and strong family history of diabetes	Total cohort 12/115 including HNF4A 2, GCK 4, HNF1A 3, MIDD 3
Riveline (2012) [54]	Cross sectional study, France,	n=146, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: ABCC8	None specified	Family members or adults with ABCC8 mutations plus 139 adults with diabetes well controlled on SU agents.	Patients with affected family member: 7/7 T2D controlled on sulfonylurea: 4/139
Delvecchio (2017) [55]	Cross sectional study, Italy, 93% white European, 3.4 % North African, 1.3 % African	n=240 already diagnosed monogenic diabetes, M:F NA, BMI NA	Type of genetic testing: Sanger sequencing. Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; Screened first gene based on clinical suspicion. First GCK if IFG or stable fasting hyperglycemia Max 8,3mol/L AND neg autoantibodies. If negative > HNF1A if negative >HNF4A. Severe progressive >HNF1A first. Urogenital malformations > HNF1B. PDX1, NEUROD1, INS, ABCC8, KCNJ11. Investigated last > GATA6 and INSR	Checked against Human Gene Mutation Database	Children consecutively diagnosed with diabetes or impaired fasting glucose from 2007-2012	Monogenic diabetes represented 240/3781 of the cohort including MODY cases: GCK 181, HNF1A 16, HNF4A 6, HNF1B 3; PDX1 2, INS 1, ABCC8 1; Neonatal diabetes 21 cases, genetic syndromes 9 cases
Thanabalasingham (2012) [56]	Cross sectional study, United Kingdom, 90% white British	n= 140, M:F NA, BMI NA	Type of genetic testing: Sanger sequencing. Genes sequenced: HNF1A; GCK; HNF4A	None specified	Young Diabetes in Oxford Study: diagnosed up to 45 years and investigated if met certain clinical criteria for MODY.	HNF1A-MODY was found in 2/20 patients with Clinically Defined T1D with evidence of residual beta-cell function, 13/80 patients with clinically defined T2D with either onset<30years or absence of metabolic syndrome

Lorini (2009) [57]	Cohort study, Other: Italy, Italian	n=172, M:F , BMI GCK 17(14-24);HNF1A 21 (13-25);cases without GCK or HNF1A 17(16-20)	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A; GCK	Local lab guidelines	Multicenter study on incidental hyperglycemia, diagnosed up to age 25	GCK 109/172 HNF1A 12/172
Pavić (2018) [58]	Cross sectional study, Croatia, Croatian	n=477, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A	Local lab guidelines	Adults diagnosed up to 45 years, HNF1A sequencing in all antibody negative, C-peptide positive individuals. Strict pathogenicity criteria.	Yield 8/477 (1.7%). Estimated prevalence of HNF1A-MODY in Croatia of 66 per million.
Juszczak (2019) [59]	Cohort study, United Kingdom, UK and Croatia	n=989, M:F 587:402, BMI HNF1A-MODY 25.5+/-9.4 : no variant 30.4+/-8.3	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A	ACMG	Young Diabetes in Oxford Study: diagnosis up to 45 years, fasting C-peptide $\geq$ 0.2 nmol/L, negative GAD antibodies. CRP and plasma glycans assessed as biomarkers.	All probands: 16/989 (1.6%); Using CRP<0.81, 14/269 (5%), sensitivity 88%, specificity 69%; Strict MODY criteria 8/99 (8%), sensitivity 50%; MODY calculator probability>20%: 9/136 (6.6%), sensitivity 56%
Demus (2022) [60]	Case control study, Croatia (n=501) and UK (n=499), UK and Croatia	n=947, M:F 540:407, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A	ACMG	Diabetes diagnosed up to 45 years, islet antibody negative and C-peptide positive, all HNF1A sequenced and variants classified and tested against a plasma glycan biomarker plate assay constructed for the glycan pattern associated with HNF1A-MODY	Likely damaging variant vs no HNF1A variant: ROC curve C statistic 0.87
Tatsi (2013) [61]	Cohort study, Greece, Greek	n=395, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A	Bioinformatics	Clinically suspected MODY diagnosed up to 25 years, referred for diagnostic testing	Overall yield 88/395 (22%)

Szopa (2016) [62]	Cross sectional study, Poland, Polish	n=156, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: NEUROD1	None specified	Clinically suspected MODY diagnosed up to 30 years, recruited at University Hospital, Krakow, Poland; negative for HNF1A and/or GCK based on clinical presentation	Yield 1/156 (0.6%)
Skupien (2008) [63]	Case control study, Other: Poland, Polish	n=no new sequencing, M:F NA, BMI HNF1A-MODY 23+/-3.4 T2D 35.1 +/- 7.9	Type of genetic testing: No new sequencing. Genes sequenced: Biomarker study for 1,5AG levels in HNF1A-MODY	None specified	HNF1A-MODY cases, T2D and non-diabetic control groups.	Biomarker study: 1,5 AG could discriminate HNF1A-MODY from T2D with a ROC C-statistic of 0.73, sensitivity 73%, specificity 65%
Molven (2008) [64]	Cohort study, Norway,	n=315, M:F NA, BMI NA	Type of genetic testing: Single gene. Genes sequenced: INS (in those negative for HNF1A, GCK, KCNJ11)	None specified	Two populations based registries NCDR and The Norwegian MODY registry. Children from NCDR are <18 yrs. Subjects from the MODY registry can have any age if at least 2 criteria are fulfilled	Overall yield 2/315(0.6%); NCDR 1/124 (0.8%); MODY registry 1/62 who met all MODY criteria.
Bellanné-Chantelot (2011) [65]	Cohort study, France, French	n=487, M:F 228 :251, BMI NA	Type of genetic testing: Sanger sequencing. Genes sequenced: HNF1A, GCK, HNF4A	Local lab guidelines	Referrals with a strong clinical suspicion of MODY because of a clinical suspicion of HNF1A-MODY, based on a diagnosis of diabetes at age < 40 years, a family history of diabetes in at least two generations and the absence of obesity.	HNF1A-MODY: 196/487 (40%).



Thanabalasingham (2011) [66]	Cross sectional study, Other: UK, France, Denmark, Finland, Slovakia, Poland, Norway, European	n=1497, M:F Summary data not available, BMI Summary data not available	Type of genetic testing: No new sequencing. Genes sequenced: investigation of CRP levels in MODY subtypes	None specified	Individuals with HNF1A-MODY, GCK-MODY, HNF4A-MODY or T2D diagnosed <=45 yrs	Biomarker study: hsCRP discriminated HNF1A-MODY from T2D with a ROC C-statistic of 0.79-0.97.
Shields 2012 [67]	Case control study, UK, White European	n=594, M:F 473:718, BMI NA	Type of genetic testing: large NGS panel, Genes sequenced: HNF1A, HNF4A, GCK	ACMG	Individuals referred for MODY testing in national UK centre diagnosed up to 35 years. MODY probability model derived by logistic regression comparing MODY groups with gold standard T1D and T2D	Any MODY vs T1D: ROC C-statistic 0.95, 87% sensitivity and 88 specificity for a probability of 40%. Any MODY vs T2D: ROC C-statistic 0.98, Sensitivity 92%, Specificity 95% for a probability of 60%
Szopa (2019) [68]	Case control study, Other: Poland, Polish	n=165, M:F 157 :199, BMI	Type of genetic testing: No new sequencing. Genes sequenced: Investigation of biomarkers in HNF1A; GCK	None specified	Cases of 77 HNF1A, 88 GCK, controls: 99 T1D, 91 T2D	Testing a decision algorithm using several biomarkers. 92.9% of T1D, 84.8% of T2D, 64.9% of HNF1A-MODY, and 52.3% of GCK-MODY were correctly identified, C-peptide and clinical features performed best and overall MODY subgroups could not be discriminated with the model.
Pal (2010) [69]	Cohort study, United Kingdom, 90% White British	n=no new genetic sequencing, M:F NA, BMI NA	Type of genetic testing: No new sequencing. Genes sequenced: Investigation of 1,5AG levels in HNF1A; GCK; HNF4A	None specified	Participants with known MODY (HNF1A or GCK) and Type 1, LADA and Type 2 diabetes who underwent measurement of 1,5 AG. This is a replication study.	Biomarker study of 1,5AG levels. 1,5AG is lower in HNF1A-MODY than T2D and higher in GCK-MODY than other groups, ROC C-statistic 0.79 for GCK-MODY vs T2D.
Patel 2022 [70]	Cross-sectional study from seven paediatric diabetes clinics across	n=236, M:F NA, BMI NA	Type of genetic testing: Large Monogenic Diabetes Panel. Genes Sequenced: ABCC8, AGPAT2, AKT2, APPL1, BSCL2, CISD2, CEL, COQ2,	None specified	Combination of T1D-GRS and autoantibody status to select 236 children with high to moderate likelihood of monogenic diabetes (111	34/236 including 11 GCK, 3 HNF1A, 1 HNF4A, 2 HNF1B, 1 KCNJ11, 2 INS, 1 m.3243A>G,

	Turkey; European ancestry		<i>CTLA4, EIF2AK3, FOXP3, GATA4, GATA6, GCK, GLIS3, HNF1A, HNF4A, HNF1B, IER3IP1, IL2RA, INS, INSR, ITCH, KCNJ11, LMNA, LRBA, MNX1, NEUROD1, NEUROG3, NKX2-2, m.3243A&gt;G, PAX6, PCBD1, PDX1, PIK3R1, PLIN1, POLD1, PPARG, PTF1A, RFX6, SIRT1, SLC2A2, SLC19A2, SLC29A3, STAT1, STAT3, STAT5B, TRMT10A, WFS1, ZFP57</i>		children with low T1D-GRS irrespective of islet autoantibody status and 125 islet-autoantibody-negative children with moderate T1D GRS	1 PTF1A, 7 WFS1, 3 SLC19A2, 1 SLC29A3, 1 TRMT10A
Besser (2011) [71]	Case control study, United Kingdom,	n=, M:F 90:110, BMI NA	Type of genetic testing: No new sequencing. Genes sequenced: Investigation of Urinary C-Peptide levels in HNF1A-MODY	None specified	Individuals with known MODY compared to T1 and T2	Biomarker study of Urinary C-peptide. ROC C-statistic 0.98 for discriminating long duration T1D from HNF1A/4A-MODY
Flannick (2013) [72]	Cohort study, European and African American	n=4003, M:F 1745:2259, BMI range 23.6 to 34.2 depending on cohort	Type of genetic testing: Large MODY panel. Genes sequenced: HNF1A, GCK, HNF4A, HNF1B, PDX1, INS, NEUROD1	In-house rules using computational prediction and prior reports	Individuals drawn from three population-based cohorts including Framingham Heart Study Offspring cohort (randomly ascertained 1541), Jackson Heart Study (1691), and extremes of T2D genetic risk from Finnish and Swedish cohorts (771).	Overall yield 121/4003 (0.03%) 13 Nonsynonymous MAF>1% and 108 Nonsynonymous MAF <1% of which 21 possibly pathogenic, 25 HGMD (Human Gene Mutation Database), 6 Putative pathogenic
Weinreich (2015) [73]	Cross sectional study, Netherlands, European	n=1319, M:F NA, BMI NA	Type of genetic testing: Single. Genes sequenced: HNF1A, HNF4A, GCK	None specified	People with clinically suspected MODY referred to molecular testing centre over 10 years	Any MODY: 502/1319 (38%) including HNF1A 222 and GCK 204
<b>Monogenic Diabetes: Non-European</b>						
HuaTan (2022) [74]	Cohort study, Singapore	n=267, M:F NA, BMI <32.5	Type of genetic testing: Large MODY panel (>= 5 genes). Genes sequenced: HNF1B	None specified	Diabetes diagnosed up to age 35 with a clinical suspicion of MODY (BMI<32.5, islet antibody negative).	40/267 (15%) diagnosed with MODY including 4/267 (1.5%), <i>HNF1B</i>

Kleinberger (2018) [75]	Cohort study, United States, Hispanic, non-Hispanic white, non-Hispanic black	n=488, M:F 177:311, BMI Z-score:2.31±0.41	Type of genetic testing: Large MODY panel (>= 5 genes). Genes sequenced: 40 autosomal genes known or predicted to cause monogenic diabetes, including 13 known MODY genes	ACMG	TODAY cohort: adolescents age 10–17 diagnosed with T2D within 2 years of study enrollment, C-peptide present, islet antibodies absent	Overweight/obese adolescents diagnosed with type 2 diabetes (T2D): 22/488 including HNF4A (7), GCK (7), HNF1A (5), INS (2), KLF11 (1)
Mifsud (2022) [76]	Cohort study, France, Multiple ethnicities	n=1975, M:F 937:1038, BMI NA	Type of genetic testing: Large MODY panel (>= 5 genes). Genes sequenced: GCK, HNF1A, HNF4A, HNF1B, ABCC8, KCNJ11, INS	ACMG	Adult probands (42% non-EuroCaucasians), selected on the absence of diabetes autoantibodies and ≥2 of the following criteria: age ≤40 years, BMI <30 kg/m2 at diagnosis, and a family history of diabetes in ≥2 generations	Absence of antibodies and 2/3 of (1) age at diabetes diagnosis ≥15 years and ≤40 years in the proband, or in at least two relatives with diabetes; (2) the absence of obesity in the proband or in at least two relatives with diabetes; (3) 2 gen family history of diabetes: 315/1975
deSantana (2019) [77]	Cohort study, Brazil, Brazilian	n=102, M:F NA, BMI NA	Type of genetic testing: Large MODY panel (>= 5 genes). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; PDX1, NEUROD1, CEL, INS, KCNJ11, ABCC8, APPL1	ACMG	Probands referred for MODY testing, diagnosed up to 35 years with negative testing for HNF4A, GCK, and HNF1A and deletions in HNF1B excluded	Yield 13/102 (12.7%) including 8 GCK, 1 PDX1, 2 HNF1B, 1 NEUROD1, 1 ABCC8
Mohan (2018) [78]	Cross sectional study, India and US, Southern India	n=152, M:F 96:56, BMI 24.29	Type of genetic testing: Whole exome (n=31), targeted exome (n=150). Genes sequenced: Exome	None specified	Clinically diagnosed with MODY, up to 30 years at diagnosis	<30 years, negative for auto antibodies, three-generation family history: 39/152 including HNF1A: 11/152, ABCC8: 5/152
Breidbart (2021) [79]	Cross sectional study, United States, Asian 10.6%, Black 3.1%, European 53.1%, Latina 23.8%, mixed 7.5%	n=160, M:F 84:76, BMI NA	Type of genetic testing: GCK/HNF1A followed by Exome sequencing. Genes sequenced: GCK and HNF1A first	ACMG	Probands referred to MODY registry, neonatal diabetes diagnosed up to 12 months excluded	Yield of full selected cohort: 60/160 including GCK (45), HNF1A (11), HNF4A (1), PDX1 (1), KCNJ11 (1), HNF1B (1)

Giuffrida (2017) [80]	Cohort study, Brazil, Brazilian	n=311, M:F 64% males (GCK probands). 40% males (HNF1A probands), BMI 19 ±6 (GCK, probands only), 25±6(HNF1A, probands only)	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A; GCK	None specified	Multicentre study of 140 probands with clinical characteristics of MODY	Clinical profile consistent with MODY in Brazilian probands and families: Total 103/311 including 72 GCK, 31 HNF1A
Tonooka (2002) [81]	Cohort study, Japan, Japanese	n=203, M:F 79:124, BMI 23.7 +/- 6	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A	None specified	Non-type 1 diabetes dx before 15 years of age. Glycosuria picked up by annual school health exam.	Yield 18/203
Horikawa (2014) [82]	Cross sectional study, Japan, Japanese	n=230, M:F 103:127, BMI 21.8	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A; HNF1B	None specified	Suspected MODY, onset up to 35 yrs, islet antibody negative, BMI <30	Diabetes diagnosis <= 35 years, antibody negative: 30/230
Karaca (2017) [83]	Cross sectional study, Turkey, Turkish	n=136, M:F 65:71, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A	Bioinformatics	Clinically suspected MODY with age of onset up to 49 years, Islet antibody absent and family history of diabetes	Yield for strict MODY criteria 10/136 (7.35%)
Li (2021) [84]	Cross sectional study, Other: China, Han Chinese	n=543, M:F 375:168, BMI probands 27.6 ± 4.9 controls 25.8 ± 3.5	Type of genetic testing: Customized gene panel for ABCC8 and exon capture. Genes sequenced: ABCC8	ACMG	Diagnosed with diabetes up to 40 years, antibody negative, C-peptide positive and without Mitochondrial 3243 variant	Yield 8/543 (1.8%)
Xu (2005) [85]	Cohort study, China, Chinese	n=146, M:F NA, BMI NA	Type of genetic testing: Single. Genes sequenced: HNF1A, HNF4A, GCK	None specified	Clinically suspected MODY with age of diagnosis <25years from diabetes clinics in Hong Kong	Any MODY 15/146 (10%) including HNF1A 13 cases, GCK 2 cases, HNF4A 0 cases

Yaghootkar (2019) [86]	Cross sectional study, Iran/UK, Iranian	n=127, M:F 63:64, BMI NA	Type of genetic testing: Large MODY panel. Genes sequenced: 35 gene panel	ACMG	Children diagnosed 9months-5years from 2 hospital clinics, 32% consanguineous	Any MODY 6/126 (4.7%) including 1 GCK, 3 WFS1, 1 SLC19A2, 1 SLC29A3. T1GRS <15th centile for T1D identified all MODY Cases, 100% sensitive, 82% specific, ROC C-statistic 0.9. MODY cases were islet antibody negative.
Yamada (1997) [87]	Cross sectional study, Japan, Japanese	n=103, M:F NA, BMI 22+/-2.2	Type of genetic testing: Single. Genes sequenced: HNF1A	None specified	Diagnosed >40years, attending a diabetes clinic	0/103 (1 VUS)
Yang (2006) [88]	Case-control study, China, Chinese	n=192, M:F 54:40, BMI 24.2+/-0.78	Type of genetic testing: Single. Genes sequenced: HNF1A	In-house rules, local control group. Some doubt over VUS.	Attending the Shanghai Diabetes Institute, not clinically T1D. Group A diag<40years, 1 relative with DM, Group B diag>40years, 3 gen FH	Whole group 3/192 (1.6%); young onset 2/94; older-onset familial 1/98
Yorifuji (2018) [89]	Cohort study, Japan, Japanese	n=263, M:F NA, BMI median 45th centile	Type of genetic testing: Single . Genes sequenced: Sequential approach: Mt3243A>G, GCK-MODY, HNF1A, HNF4A, HNF1B, other genes if specific features	None specified	Clinically suspected MODY referred for genetic testing: <30years, islet antibody negative, CP present, non-obese, + group with incidental hyperglycaemia	Overall: 103/263 (39%) including Mt3243A.G 4, GCK 57, HNF1A 29, HNF4A 7, HNF1B 10, other 13

Zmyslowska 2022 [90]	Cohort study, Polish, European	n=542 probands, 290:252, BMI NA	<i>Type of genetic testing: Large Monogenic Diabetes Panel. Genes sequenced: ABCC8, AIRE, APPL1, BLK, CISD2, CEL, EIF2AK3, FOXP3, GATA4, GATA6, GCK, GCKR, GLIS3, GLUD1, HADH, HNF1A, HNF4A, HNF1B, INS, ISL1, KCNJ11, KLF11, MAFA, MAFB, MNX1, NEUROD1, NEUROG3, NKX2-2, NKX6-1, PAX4, PAX6, PDX1, PTF1A, RFX6, WFS1</i>	ACMG	Referred to the Genetic Outpatient Clinic in Poland from 12 Polish Diabetes Centers, with presence of hyperglycaemia or diabetes mellitus, positive family history of diabetes, absence of autoantibodies, preserved insulin secretion based on fasting C-peptide or insulin values and absence of additional organ-specific symptoms.	Overall Yield 192/542 including GCK 148, HNF1A 19, HNF4A 5, HNF1B 6, ABCC8 2, KCNJ11 8, RFX6 1, PDX1 5, WFS1 1, MAFA 1, APPL1 3
<b>HNF1B</b>						
Wang (2012) [91]	Cohort study, China, Chinese	n=104, M:F 74:30, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1B	Local lab guidelines	Proband from Shanghai Diabetes Institute, mean age 64.7+/-13.7 years, negative autoantibodies and either renal structural abnormalities or impaired renal function	Overall yield 3/104 (2.9%)
Faguer (2014) [92]	Cohort study, France,	n=433, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1B	None specified	Cohort with known HNF1B-MODY, clinical features used to derive an "HNF1B-score" (using previously published data), 65% aged <=16years	For an HNF1B score of >8: ROC C-statistic 0.78 (0.72-0.83), sensitivity 92.2%, specificity 41.1%, NPV >99%
Clissold (2015) [93]	Cohort study, United Kingdom,	n=686, M:F 343:343, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1B	None specified	Proband referred for HNF1B testing at Exeter between 1998-2012	HNF1B score of >8, sensitivity 80%, specificity 38%, PPV 31%, NPV 85%.

Edghill (2013) [94]	Cohort study, United Kingdom,	n=124, M:F NA, BMI median 24	Type of genetic testing: HNF1B deletion via MLPA only. Genes sequenced: HNF1B	None specified	Patients referred to the Molecular Genetics Laboratory at the Royal Devon and Exeter Hospital for genetic testing to investigate a possible diagnosis of MODY, but no mutation had been found by sequence analysis.	Yield 3/124 (2.4%)
<b>Lipodystrophy</b>						
Gong (2021) [95]	Cohort study, China, Han Chinese	n=1002, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: PPARG	ACMG	T2D diagnosed 18 -40 years, islet antibody negative, C-peptide positive recruited at the Peking University People's Hospital 2014-18	Yield 6/1006 (0.6%)
Decaudain (2007) [96]	Cohort study, France, French	n=277, M:F NA, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: LMNA	None specified	Probands with suspected severe insulin resistance (lipodystrophy and/or android body habitus, insulin resistance or altered glucose tolerance) between 2002-6	Yield 27/277 (9.7%)
<b>Biomarkers</b>						

Ma (2020)[97]	case/control + cohort, China, Chinese	n=535, M:F 375:176, BMI NA	Type of genetic testing: Single gene(s). Genes sequenced: HNF1A; GCK; HNF4A; HNF1B; MT3243A>G	ACMG	Control groups of normoglycaemia, early-onset diabetes (diagnosed at 14–40 years) and HNF1A-MODY were used to define normal ranges for clinical biomarkers (body mass index (BMI), HDL-c and hsCRP). A second group with early onset diabetes were used to validate the effectiveness of the biomarkers established in this study for HNF1A-MODY	Used HNF1A-Clinical screening strategy in cohort of 410 subjects with young onset type 2 diabetes meeting 3 or 4 biomarker criteria for BMI<28 kg/m2, hs-CRP <0.75 mg/L, Fasting insulin <102 pmol/L and HDL-c >1.12 mmol/L levels received genetic testing and yield 17/182.
McDonald (2011) [98]	Cohort study, United Kingdom, European	n=540, M:F NA, BMI NA	Type of genetic testing: No new sequencing. Genes sequenced: Investigation of hsCRP in MODY subtypes	<i>None specified</i>	540 patients with a confirmed genetic dx of MODY (220 HNF1A, 245 GCK, 54 HNF4A, and 21 HNF1B). 53 patients with T1D and 157 with T2D	Biomarker study: replication of hsCRP levels. hsCRP was lower in HNF1A-MODY than T2D, T1D, HNF4A-MODY, GCK-MODY and HNF1B-MODY. ROC C-statistic 0.84 HNF1A-MODY vs T2D
McDonald (2011) [99]	Case control study, United Kingdom,	n=508, M:F NA, BMI NA	Type of genetic testing: No new sequencing. Genes sequenced: Investigation of prevalence of islet antibodies in MODY	<i>None specified</i>	Antibody status was investigated in participants with a confirmed genetic diagnosis of MODY (263 probands and 245 family members): 227GCK, 229HNF1A and 52HNF4A. In addition, serum from 98 patients (median age of 15 years ;) diagnosed with Type 1 diabetes within the past 6 months was analyzed. Fifty samples were from the Bart's-Oxford (BOX) family study and 48 from the Diabetes Autoantibody Standardization Programme. To establish an antibody titre cut-off for GAD and IA-2antibodies, we tested 500 routine clinical samples of patients aged between 18 and 75 years	Antibodies found in 5/508 (<1%) of those with MODY



					without a clinical history of diabetes and an HbA1c level of less than 6.0% (42 mmol/mol).	
McDonald (2012) [100]	Cohort study, United Kingdom,	n=564, M:F 327:237, BMI NA	Type of genetic testing: No new sequencing. Genes sequenced: Study of lipid biomarkers in HNF1A-MODY	None specified	Individuals with HNF1A, non-diabetic and T2D	Biomarker study: HDL-Chol was the best lipid measurement to discriminate HNF1A-MODY from T2D, ROC C-statistic 0.76, sensitivity 75%, specificity 64%

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**Supplementary Table 4: Complete set of papers extracted for question 2. How to test for monogenic diabetes**

Study Details	Individuals tested	Test methodology and number of different genes tested	Genes analysed	Individuals diagnosed, diagnostic yield and number of different genetic subtypes diagnosed	Number of patients diagnosed by subtype:
Abbasi, 2018 Iran [1]	60 neonates with NDM	Sanger sequencing; 4	<i>ABCC8</i> ; <i>EIF2AK3</i> ; <i>INS</i> ; <i>KCNJ11</i>	11 (18%); all <i>EIF2AK3</i>	11 <i>EIF2AK3</i>
Al-Senani, 2018 Oman [2]	18 neonates with NDM	tNGS (RNA baits) and MS-PCR; 24	<i>6q24</i> ; <i>ABCC8</i> ; <i>EIF2AK3</i> ; <i>FOXP3</i> ; <i>GATA4</i> ; <i>GATA6</i> ; <i>GCK</i> ; <i>GLIS3</i> ; <i>HNF1B</i> ; <i>INS</i> ; <i>KCNJ11</i> ; <i>IER3IP1</i> ; <i>IL2RA</i> ; <i>LRBA</i> ; <i>NEUROD1</i> ; <i>NEUROG3</i> ; <i>NKX2-2</i> ; <i>PDX1</i> ; <i>PTF1A</i> ; <i>RFX6</i> ; <i>SLC2A2</i> ; <i>SLC19A2</i> ; <i>STAT3</i> ; <i>WFS1</i> ; <i>ZFP57</i>	9 (50%); 2	5 <i>GCK</i> , 1 <i>KCNJ11</i>
Al-Kandari, 2021 Kuwait [3]	31 children with suspected MODY	MLPA and targeted exome sequencing (gene panel); 22	<i>ABCC8</i> ; <i>CISD2</i> ; <i>CEL</i> ; <i>GATA6</i> ; <i>GCK</i> ; <i>HNF1A</i> ; <i>HNF4A</i> ; <i>HNF1B</i> ; <i>INS</i> ; <i>INSR</i> ; <i>KCNJ11</i> ; <i>LMNA</i> ; <i>NEUROD1</i> ; m.3243A>G; <i>PAX6</i> ; <i>PDX1</i> ; <i>PLIN1</i> ; <i>PPARG</i> ; <i>RFX6</i> ; <i>WFS1</i> ; <i>ZFP57</i>	7 (23%); 5	1 <i>GCK</i> , 2 <i>HNF1A</i> , 1 <i>HNF4A</i> , 2 <i>HNF1B</i> , 1 <i>PDX</i>
Al-Khawaga, 2019 Qatar [4]	7 neonates with NDM	WES (gene agnostic), WGS (gene agnostic) and CNV analysis as part of tNGS/exome/genome sequencing; Not Stated	Whole exome; Whole genome	7 (100%); 6	1 <i>GCK</i> , 1 <i>HNF1B</i> , 2 <i>INS</i> , 1 <i>EIF2AK3</i> , 1 <i>PTF1A</i>
Alkorta-Aranburu, 2014 USA [5]	44 children and adults with suspected MODY and 32 with neonates with NDM	WES (gene agnostic), WGS (gene agnostic) and CNV analysis as part of tNGS/exome/genome sequencing; Not Stated	<i>ABCC8</i> ; <i>AKT2</i> ; <i>ALMS1</i> ; <i>BLK</i> ; <i>CISD2</i> ; <i>CEL</i> ; <i>CP</i> ; <i>DCAF17</i> ; <i>EIF2AK3</i> ; <i>FOXP3</i> ; <i>GATA6</i> ; <i>GCK</i> ; <i>GLIS3</i> ; <i>GLUD1</i> ; <i>HADH</i> ; <i>HNF1A</i> ; <i>HNF4A</i> ; <i>HNF1B</i> ; <i>IER3IP1</i> ; <i>INS</i> ; <i>INSR</i> ; <i>KCNJ11</i> ; <i>NEUROD1</i> ; <i>NEUROG3</i> ; <i>PAX4</i> ; <i>PAX6</i> ; <i>PDX1</i> ; <i>PTF1A</i> ; <i>RFX6</i> ; <i>SLC2A2</i> ; <i>SLC19A2</i> ; <i>SLC29A3</i> ; <i>TBC1D4</i> ; <i>WFS1</i> ; <i>ZFP57</i>	12 with MODY (27%); 2 and 7 with NDM (22%); 5	11 <i>GCK</i> , 2 <i>HNF1A</i> , 1 <i>ABCC8</i> , 2 <i>KCNJ11</i> , 2 <i>INS</i> , 1 <i>EIF2AK3</i>
Alkorta-Aranburu, 2016 USA [6]	22 neonates with NDM	MS-MLPA and tNGS (RNA baits); 11	<i>6q24</i> ; <i>ABCC8</i> ; <i>EIF2AK3</i> ; <i>FOXP3</i> ; <i>GATA4</i> ; <i>GCK</i> ; <i>INS</i> ; <i>KCNJ11</i> ; <i>MXN1</i> ; <i>NKX2-2</i> ; <i>PDX1</i> ; <i>ZFP57</i>	14 (64%); 5	2 <i>ABCC8</i> , 2 <i>KCNJ11</i> , 1 <i>INS</i> , 1 <i>FOXP3</i> , 1 <i>6q24</i>
Ang, 2016 Singapore [7]	84 adults with suspected MODY	tNGS (PCR using Ion AmpliSeq) and Genotyping (TaqMan); 16	<i>ABCC8</i> ; <i>BLK</i> ; <i>CEL</i> ; <i>GCK</i> ; <i>HNF1A</i> ; <i>HNF4A</i> ; <i>HNF1B</i> ; <i>INS</i> ; <i>INSR</i> ; <i>KCNJ11</i> ; <i>KLF11</i> ; <i>LMNA</i> ; <i>NEUROD1</i> ; m.3243A>G; <i>PAX4</i> ; <i>PDX1</i> ; <i>PPARG</i>	13 (16%); 7	1 <i>GCK</i> , 4 <i>HNF1A</i> , 1 <i>HNF4A</i> , 1 <i>ABCC8</i> , 1 <i>KCNJ11</i> , 2 m.3243A>G
Anik, 2015 Turkey [8]	42 children with suspected MODY	tNGS (PCR using Illumina Nextera XT); 11	<i>BLK</i> ; <i>CEL</i> ; <i>GCK</i> ; <i>HNF1A</i> ; <i>HNF4A</i> ; <i>HNF1B</i> ; <i>INS</i> ; <i>KLF11</i> ; <i>NEUROD1</i> ; <i>PAX4</i> ; <i>PDX1</i>	12 (29%); 5	8 <i>GCK</i> , 1 <i>HNF1A</i> , 1 <i>HNF1B</i> , 1 <i>PDX1</i> , 1 <i>BLK</i>
Antosik, 2016 Poland [9]	1 neonate with NDM	tNGS (RNA baits); 1	<i>GCK</i>	1 (100%); 1	1 <i>GCK</i>

Ateş, 2021 Turkey [10]	182 adults with suspected MODY	tNGS (PCR using Agilent MODY-MASTR assay); 7	ABCC8; GCK; HNF1A; HNF4A; HNF1B; INS; KCNJ11	30 (17%), 6	10 GCK, 9 HNF1A, 2 HNF4A, 2 HNF1B, 6 ABCC8, 1 KCNJ11
Bansal, 2017 USA [11]	4016 adults with type 2 DM	tNGS (RNA baits); 22	ABCC8; BLK; CEL; EIF2AK3; GATA6; GCK; GLIS3; HNF1A; HNF4A; HNF1B; INS; KCNJ11; KLF11; NEUROD1; NEUROG3; PAX4; PAX6; PDX1; PPARG; RFX6; SLC19A2; WFS1	53 (1%), 8	21 GCK, 17 HNF1A, 5 HNF4A, 1 HNF1B, 6 ABCC8, 1 INS, 1 WFS1, 1 PPARG
Berberich, 2021 Canada [12]	57 children and adults with suspected MODY	tNGS (DNA baits) and CNV analysis as part of tNGS; 14	ABCC8; CEL; GCK; HNF1A; HNF4A; HNF1B; INS; INSR; KCNJ11; LMNA; NEUROD1; PDX1; PPARG; RFX6	3 (5%), 1	3 HNF1B
Carette, 2010 France [13]	84 children and adults with suspected MODY	Sanger sequencing and MLPA; 2	HNF1A; HNF4A	8 (10%), 2	2 HNF1A, 6 HNF4A
Caswell, 2020 UK [14]	33 at-risk pregnancies	Droplet digital PCR; 1	GCK	21 (64%), 1	21 GCK
Chambers, 2016 USA [15]	97 children and adults with suspected MODY	Sanger sequencing; 5	GCK; HNF1A; HNF4A; HNF1B; PDX1	20 (21%), 3	8 GCK, 9 HNF1A, 3 HNF4A
Colclough, 2022 UK [16]	1280 children and adults with suspected MODY	tNGS (RNA baits) and CNV analysis as part of tNGS; 27	ABCC8; CISD2; CEL; GATA4; GATA6; GCK; HNF1A; HNF4A; HNF1B; INS; INSR; KCNJ11; LMNA; NEUROD1; m.3243A>G; PAX6; PCBD1; PDX1; PLIN1; POLD1; PPARG; RFX6; SLC29A3; TRMT10A; WFS1; ZBTB20; ZFP57	297 (23%), 17	66 GCK, 98 HNF1A, 42 HNF4A, 18 HNF1B, 11 ABCC8, 5 KCNJ11, 6 INS, 8 RFX6, 3 NEUROD1, 2 PDX1, 24 m.3243A>G, 6 WFS1, 4 INSR, 1 PPARG, 1 TRMT10A, 1 SLC29A3, 1 GATA6
De Franco, 2015 UK [17]	1020 neonates with NDM	Sanger sequencing, MS-MLPA) and tNGS (RNA baits) and CNV analysis as part of tNGS; 23	6q24; ABCC8; EIF2AK3; FOXP3; GATA4; GATA6; GCK; GLIS3; HNF1B; IER3IP1; INS; KCNJ11; IER3IP1; MNX1; NEUROD1; NEUROG3; NKX2-2; PDX1; PTF1A; RFX6; SLC2A2; SLC19A2; ZFP57	840 (82%), 22	30 GCK, 2 HNF1B, 150 ABCC8, 240 KCNJ11, 110 INS, 1 RFX6, 3 NEUROD1, 6 PDX1, 76 EIF2AK3, 22 PTF1A, 14 FOXP3, 113 6q24, 7 SLC19A2, 4 GATA6, 9 GLIS3, 1 IER3IP1, 1 MNX1, 1 NEUROG3, 2 NKX2-2, 6 SLC2A2, 12 ZFP57
Donath, 2019 France [18]	1564 children and adults with suspected MODY	MLPA and tNGS (PCR using Agilent MODY-MASTR assay); 7	ABCC8; GCK; HNF1A; HNF4A; HNF1B; INS; KCNJ11	254 (16%), 7	109 GCK, 82 HNF1A, 25 HNF4A, 15 HNF1B, 8 ABCC8, 3 KCNJ11, 7 INS,
Ellard, 2013 UK [19]	33 children with suspected MODY and 49 neonates with NDM	tNGS (RNA baits) and CNV analysis as part of tNGS; 29	ABCC8; BLK; CEL; EIF2AK3; FOXP3; GATA4; GATA6; GCK; GLIS3; HNF1A; HNF4A; HNF1B; INS; KCNJ11; KLF11; IER3IP1; LMNA; NEUROD1; NEUROG3; m.3243A>G; PAX6; PDX1; PPARG; PTF1A; RFX6; SLC2A2; SLC19A2; WFS1; ZFP57	5 with MODY (15%), 4 and 9 with NDM (18%), 6	3 GCK, 1 HNF4A, 1 HNF1B, 1 ABCC8, 1 PDX1, 2 m.3243A>G, 1 EIF2AK3, 2 SLC19A2, 2 GATA6

Ellard, 2007 UK [20]	90 children and adults with suspected MODY	MLPA; 3	GCK; HNF1A; HNF4A	6 (7%), 2	1 GCK, 5 HNF1A
Johansson, 2012 Norway [21]	9 children and adults with suspected MODY	targeted exome sequencing (gene panel); 109	ABCC8; BLK; CISD2; CEL; EIF2AK3; GATA4; GATA6; GCK; GLIS3; HADH; HNF1A; HNF4A; HNF1B; INSR; KCNJ11; KLF11; LMNA; MNX1; NEUROD1; NEUROG3; NKX2-2; PAX4; PAX6; PDX1; POLD1; PPARG; PTF1A; RFX6; SLC2A2; WFS1	3 (33%), 3	1 HNF4A, 1 ABCC8, 1 PPARG
Laimon, 2021 Egypt [22]	26 neonates with NDM	Sanger sequencing, tNGS (RNA baits) and CNV analysis as part of tNGS; 22	ABCC8; EIF2AK3; FOXP3; GATA4; GATA6; GCK; GLIS3; HNF1B; INS; KCNJ11; IER3IP1; NEUROD1; NEUROG3; NKX2-2; PDX1; PTF1A; RFX6; SLC2A2; SLC19A2; STAT3; WFS1	14 (54%), 7	1 GCK, 2 ABCC8, 2 KCNJ11, 4 INS, 3 EIF2AK3, 1 SLC19A2, 1 INSR
Patel, 2022 Greece [23]	236 children with suspected MODY	tNGS (RNA baits) and CNV analysis as part of tNGS; 51	ABCC8; AGPAT2; AKT2; APPL1; BSCL2; CISD2; CEL; COQ2; CTLA4; EIF2AK3; FOXP3; GATA4; GATA6; GCK; GLIS3; HNF1A; HNF4A; HNF1B; IER3IP1; IL2RA; INS; INSR; ITCH; KCNJ11; LMNA; LRBA; MNX1; NEUROD1; NEUROG3; NKX2-2; m.3243A>G; PAX6; PCBD1; PDX1; PIK3R1; PLIN1; POLD1; PPARG; PTF1A; RFX6; SIRT1; SLC2A2; SLC19A2; SLC29A3; STAT1; STAT3; STAT5B; TRMT10A; WFS1; ZFP57	34 (14%), 12	11 GCK, 3 HNF1A, 1 HNF4A, 2 HNF1B, 1 KCNJ11, 2 INS, 1 m.3243A>G, 1 PTF1A, 7 WFS1, 3 SLC19A2, 1 SLC29A3, 1 TRMT10A
Patouni, 2021 Greece [24]	1 child with type 1 DM	Sanger sequencing and MLPA; 3	GCK; HNF1A; HNF1B	1 (100%), 2	1 HNF1A, 1 HNF1B
Pruhova, 2010 Czech Republic [25]	140 children and adults with suspected MODY	Sanger sequencing and MLPA; 1	GCK	103 (74%), 1	103 GCK
Saint-Martin, 2022 France [26]	1676 children and adults with suspected MODY	tNGS (RNA baits) and CNV analysis as part of tNGS; 18	ABCC8; CISD2; GATA4; GATA6; GCK; HNF1A; HNF4A; HNF1B; INS; INSR; KCNJ11; NEUROD1; PDX1; PLIN1; RFX6; TRMT10A; WFS1	307 (18%), 13	124 GCK, 63 HNF1A, 35 HNF4A, 18 HNF1B, 8 ABCC8, 1 KCNJ11, 4 INS, 7 RFX6, 5 NEUROD1, 7 PDX1, 24 m.3243A>G, 9 WFS1, 2 INSR
Singh, 2006 UK [27]	230 adults with type 2 DM and a negative m.3243A>G result using PCR-RFLP	Genotyping (TaqMan); 1	m.3243A>G	0 (0%), 0	
Støy, 2008 USA [28]	77 neonates with NDM	Sanger sequencing and MS-MLPA; 4	6q24; ABCC8; INS; KCNJ11	23 (30%), 3	14 KCNJ11, 7 INS, 2 6q24
Tosur, 2021 USA [29]	10 children with suspected MODY	targeted exome sequencing (gene panel); 70	ABCC8; AGPAT2; AIRE; AKT2; APPL1; BLK; BSCL2; CDKN1C; CISD2; CEL; COQ2; COQ9; CP; CTLA4; DCAF17; DNAJC3; EIF2AK3;	2 (20%), 2	1 INS, 1 RFX6



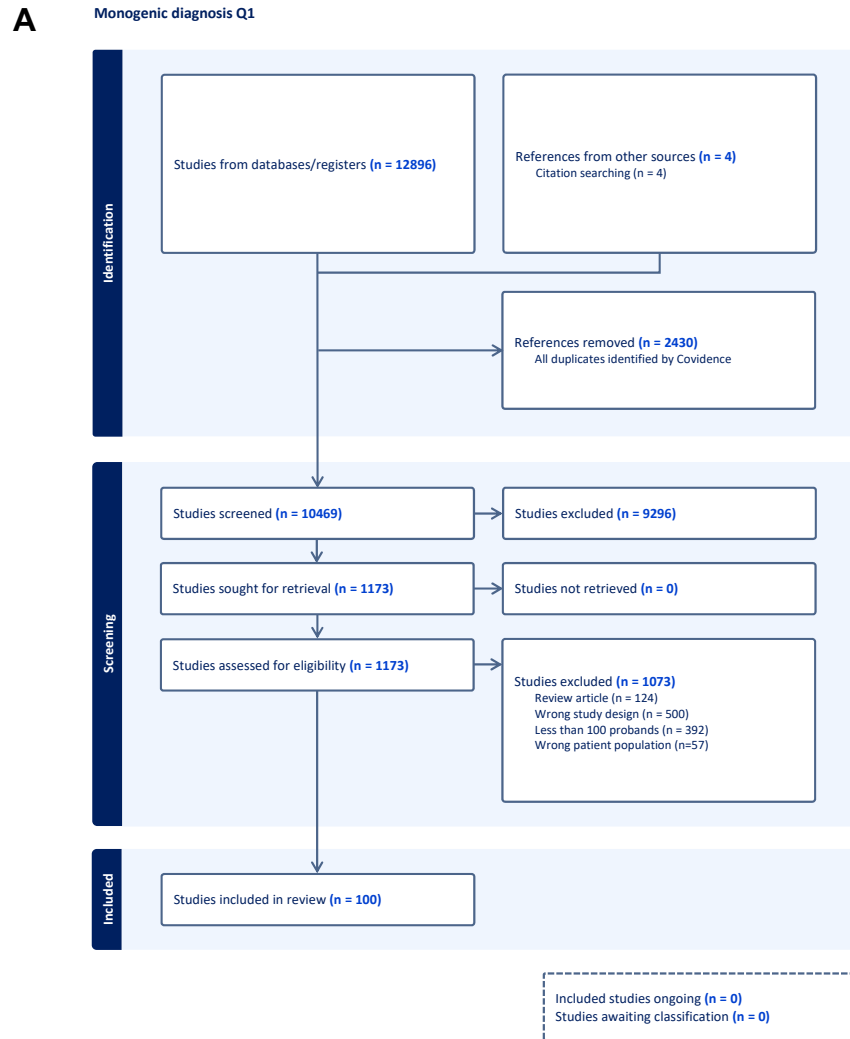
			<i>EIF2S3; FOXP3; GATA4; GATA6; GCK; GLIS3; GLUD1; HADH; HNF1A; HNF4A; HNF1B; IER3IP1; IL2RA; INS; INSR; ITCH; KCNJ11; KLF11; LMNA; LPL; LRBA; MNX1; NEUROD1; NEUROG3; NKX2; NKX2-2; m.3243A&gt;G; PAX4; PAX6; PCBD1; PDX1; PIK3R1; PLIN1; POLD1; PPARG; PTF1A; RFX6; SIRT1; SLC2A2; SLC19A2; SLC29A3; STAT1; STAT3; STAT5B; TNFAIP3; TRMT10A; WFS1; ZBTB20; ZFP57</i>		
Weedon, 2014 UK [30]	22 neonates with NDM	targeted genome sequencing (homozygosity mapping); 1	<i>PTF1A</i>	10 (48%), 1	10 <i>PTF1A</i>
Yan, 2014 China [31]	57 adults with suspected MIDD	Sanger sequencing and genotyping by Pyrosequencing, RFLP and HRM; 1	m.3243A>G	47 (83%), 1	47 m.3243A>G
Zmysłowska, 2022 Poland [32]	542 children with suspected MODY	tNGS (RNA baits); 35	<i>ABCC8; AIRE; APPL1; BLK; CISD2; CEL; EIF2AK3; FOXP3; GATA4; GATA6; GCK; GCKR; GLIS3; GLUD1; HADH; HNF1A; HNF4A; HNF1B; INS; ISL1; KCNJ11; KLF11; MAFA; MAFB; MNX1; NEUROD1; NEUROG3; NKX2-2; NKX6-1; PAX4; PAX6; PDX1; PTF1A; RFX6; WFS1</i>	198 (37%), 11	<i>GCK</i> 148, <i>HNF1A</i> 19, <i>HNF4A</i> 5, <i>HNF1B</i> 6, <i>ABCC8</i> 2, <i>KCNJ11</i> 8, <i>RFX6</i> 1, <i>PDX1</i> 5, <i>WFS1</i> 1, <i>MAFA</i> 1, <i>APPL1</i> 2

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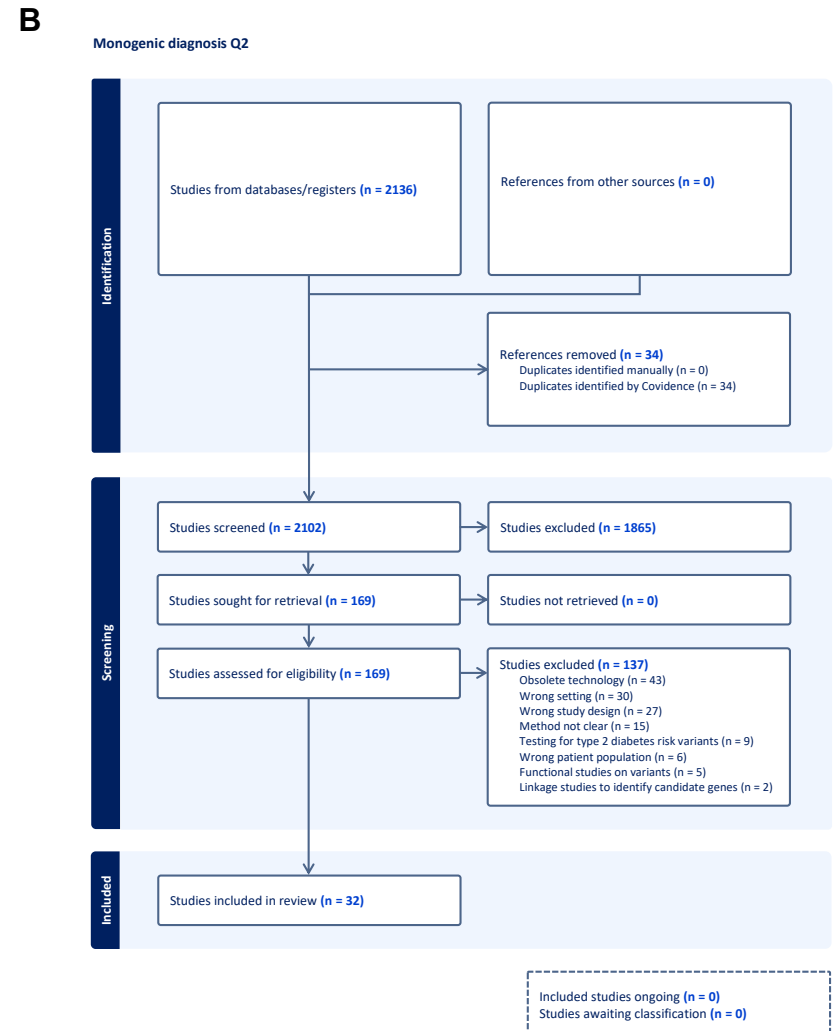
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# Supplementary Figure 1



14th April 2023



8th April 2023

