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Patient perspectives on the diagnostic journey to a monogenic diabetes diagnosis: Barriers and facilitators

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Abstract

Most monogenic diabetes is misdiagnosed as either type 1 or type 2 diabetes (T1D/T2D). Few studies have examined the diagnostic challenges from the patients' perspective. This qualitative study aimed to investigate patients' journeys to obtaining a diagnosis of maturity-onset diabetes of the young (MODY) by elucidating the range of factors that can act as barriers and facilitators throughout this process. We recruited participants from the Personalized Diabetes Medicine Program (PDMP) at University of Maryland and used respondent-driven sampling to recruit additional patients. We conducted qualitative phone interviews between October 2016 and June 2017 with nine patients with diagnoses of monogenic diabetes (one *HNF4A*-MODY, seven *GCK*-MODY, and one *HNF1A*-MODY) and one parent of a patient with *INS*-MODY. Interview data were audio recorded, transcribed, and analyzed both inductively and deductively using thematic content analysis. All patients were female, with a mean age of 35 (range: 7–67 years). The amount of time these patients were misdiagnosed ranged from a few months to 41 years. We identified barriers and facilitators in three broad themes: (a) patient-related (nature of MODY symptoms, perceived test utility, individual personality); (b) provider-related (provider awareness and knowledge, provider communication); and (c) healthcare system-related (cost of testing, access to knowledgeable providers, patient education, and support resources). The diverse range of barriers and facilitators reiterates the complexity of the MODY diagnostic process. Limited awareness and knowledge of MODY from healthcare professionals and patients themselves account for most

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AUTHOR CONTRIBUTIONS

YG contributed to study concept, acquisition of subjects, analysis and interpretation of data, and preparation of manuscript. KM involved in study concept and design, analysis and interpretation of data, and critical revision of manuscript. TP involved in the acquisition of funding, study concept and design, interpretation of data, and critical revision of manuscript. All of the authors approve the submitted version to be published. All of the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of interest

Yue Guan, Kristin A. Maloney, Toni I. Pollin declare that they have no conflict of interest.

Human studies and informed consent

The Institutional Review Board of University of Maryland School of Medicine approved this study. All persons gave their informed consent prior to their inclusion in the study.

Animal Studies

No non-human animal studies were carried out by the authors for this article.

diagnostic delays described in this study. Efforts to promote awareness of MODY and expand access to screening and testing may result in quicker diagnosis and ensure the downstream benefits of proper treatment.

Keywords

access; barriers; education; facilitators; genetic testing; MODY; monogenic diabetes; service delivery models

1 | INTRODUCTION

Approximately 2% of diabetes mellitus, or at least 500,000 cases in the United States, has a monogenic, rather than multifactorial, etiology (Hattersley et al., 2018; Pihoker et al., 2013). The most common form of monogenic diabetes is maturity-onset diabetes of the young (MODY), followed by neonatal diabetes and syndromic forms (ADA, 2016; Hattersley et al., 2018). Treatment options and prognoses for certain types of monogenic diabetes are distinct from those for type 1 and type 2 diabetes (T1D and T2D). Molecular diagnosis of the most common types of monogenic diabetes can lead to the opportunity to switch to a less invasive treatment or no treatment at all: MODY1/*HNF4A*-MODY (due to variants in the gene encoding hepatic nuclear factor 4-alpha) and MODY3/*HNF1A*-MODY (due to variants in the gene encoding hepatic nuclear factor 1-alpha), the two most common types of transcription factor MODY, can often be controlled with low-dose oral agents called sulfonylureas rather than insulin injections (Hattersley et al., 2018). MODY2/*GCK*-MODY, a stable, mild hyperglycemia resulting from a heterozygous enzyme (glucokinase) deficiency, neither responds to nor requires any treatment at all (Hattersley et al., 2018). However, the high degree of clinical overlap and other barriers mean that only 5% of patients with MODY are correctly diagnosed as such (Pihoker et al., 2013). Professional societies have begun to set forth clinical practice recommendations to promote the rate of accurate diagnosis in monogenic diabetes (American Diabetes, 2019; Hattersley et al., 2018), but these recommendations have not yet been implemented into the standard of care. Additionally, clinical genetic testing laboratories have developed multi-gene panel tests that are increasingly utilized by geneticists and endocrinologists to diagnose individuals suspected to have MODY or other forms of monogenic diabetes based on clinical and family history.

To date, few studies have investigated reasons for the diagnostic delay in monogenic diabetes. Investigations among patients who received a genetic diagnosis of MODY3/*HNF1A*-MODY showed the overall positive impact of treatment change, but also highlighted the need to address patients' fear and anxiety related to de-adoption of unwarranted insulin (Shepherd, 2010; Shepherd & Hattersley, 2004). A qualitative interview conducted by Bosma, Rigter, Weinreich, Cornel, and Henneman (2015) explored patients' reasons for taking diagnostic genetic testing for monogenic diabetes, including reassurance, reduced uncertainty, and informing at-risk family members (Bosma et al., 2015). However, they did not specifically explore barriers or opportunities during the process of obtaining a correct diagnosis.

Identifying pivotal pre-diagnostic moments on the illness trajectory is important to understand the therapeutic and psychological consequences patients experience as a result of delayed diagnosis and access to appropriate services and support. This qualitative study aimed to contribute to the scant literature regarding the patient's experience of the trajectory to receiving a diagnosis of monogenic diabetes through semi-structured telephone interviews. Specifically, we sought to explore the barriers and opportunities faced by patients during their journey to the diagnosis of MODY.

2 | METHODS

2.1 | Recruitment

We recruited participants from the Personalized Diabetes Medicine Program (PDMP) at University of Maryland (Kleinberger & Pollin, 2015; Weitzel et al., 2016) and used respondent-driven sampling to recruit additional patients. The PDMP is a genomic implementation study designed to implement, disseminate, and evaluate a sustainable approach to the identification, molecular diagnosis, and promotion of individualized therapy for monogenic forms of diabetes. The study was conducted at four distinct sites (an academic medical center, a private endocrinology practice, a Veterans Administration Hospital, and an integrated health system). Briefly, the program comprised identifying potential patients through waiting room/EHR portal questionnaires and provider/self-referrals; review of biomarkers and family and medical history, targeted next-generation sequencing; and disclosure of pathogenic and likely pathogenic variants directly to patients through a telephone genetic counseling/endocrinology consult and to providers through upload to the electronic health record (or by mail if outside the main site systems).

To be eligible for the current study, participants had to be adults (18 or older) or parents of children (0–17 years) with a diagnosis of MODY confirmed by molecular genetic testing. Participants enrolled in the PDMP project were screened for eligibility for the current study by study chart review. Eligible participants were contacted by study team members only if they indicated in the informed consent that they agreed to be re-contacted for future studies. The interviewer (YG) called or emailed prospective participants to ask if they would participate in a phone interview about their experience of receiving a diagnosis of MODY. In addition, participants who completed the interview were encouraged to share the study advertisement to other people they might know who have MODY or who are parents to an individual with MODY. Interested participants outside the PDMP project would be instructed to contact the study team members to ask questions and set up a calling time to assess eligibility and willingness to participate in the study. We approached the 15 PDMP participants enrolled at the University of Maryland site who had tested positive for MODY as of June 2017 and agreed to be contacted. Nine participants (60%) agreed to join the interview study. Only one patient was recruited through a PDMP participant via online posting. Verbal informed consent was obtained from interested participants. Recruitment ended when the research team had agreed that themes related to diagnosis barriers and facilitators had reached saturation. The Institutional Review Board of University of Maryland School of Medicine approved this study.

2.2 | Data collection

Semi-structured phone interviews were conducted between October 2016 and June 2017 with nine patients with diagnoses of MODY and one parent of a patient with MODY. We developed an interview guide informed by the Andersen Newman Behavioral Model (Andersen & Newman, 1973). Andersen conceptualized the model both as predictive and explanatory of health services use (Andersen & Newman, 1973). In this study, the health service specifically refers to the genetic test utilization for monogenic diabetes diagnosis. The model includes a broad spectrum of barriers and facilitators for obtaining a genetic diagnosis for MODY: (a) predisposing factors refer to the propensity to use monogenic diabetes genetic testing. They comprise demographic factors (e.g., age, gender), knowledge of monogenic diabetes and genetic testing, self-efficacy, and beliefs of genetic testing benefits; (b) personal, community, and institutional resources available to facilitate or hinder the uptake of genetic testing; and (c) need-based factors including the perceived need for genetic testing for monogenic diabetes from both the patient and his or her provider's perspective. Participants were also asked to provide advice for someone who might embark on the same journey as they did. We piloted the interview guide with one patient with *GCK-MODY*. Interview data were audio recorded, transcribed, and imported to NVivo 10.0 (QSR International Inc., Burlington, VT, USA) for analysis. In addition, a brief intake questionnaire that addressed patient demographic information, diabetes diagnosis, and family history of diabetes was filled out by the interviewer (YG) on the behalf of the participant by phone.

2.3 | Data analysis

We employed thematic analysis to explore participants' experiences of obtaining a diagnosis of MODY and to identify themes related to barriers and facilitators to this process. First, the interviewer (YG) carefully read all transcripts to ensure validity of the transcripts. To increase the reliability of the coding process, two coders (YG and KM) coded two interviews independently using an open coding approach, in which repeating ideas were identified and coded within each interview domain. The key domains were based on Andersen's model. Following open coding, the co-authors discussed the provisional coding schema to enhance credibility of interpretation. Barrier and facilitator codes were modified, combined, or split during discussions and the iterative coding process. Repeating themes were organized into theoretical constructs for analysis and all remaining transcripts were coded by the primary coder (YG).

3 | RESULTS

3.1 | Patient demographic and clinical characteristics

The characteristics of the 10 recruited patients are shown in Table 1. All patients were female, with a mean age of 35 (range: 7–67 years). The majority were non-Hispanic Caucasians ($n = 8$), one was African American, and one was Asian. Most patients reported having two or more blood-related relatives with diabetes. Nine participants had monogenic diabetes (one *MODY1/HNF4A-MODY*, seven *MODY2/GCK-MODY*, and one *MODY3/HNF1A-MODY*), and one was a mother of a patient with *MODY10/INS-MODY* (caused by variants in the gene encoding insulin).

3.2 | Journey of obtaining a MODY diagnosis

Prior to the MODY diagnosis, patients were diagnosed by an endocrinologist or primary care provider with T1D ($n = 1$), T2D ($n = 7$), pre-diabetes ($n = 4$), or gestational diabetes ($n = 1$). Most of the patients in this study undertook genetic testing as part of PDMP; five patients were self-referrals, while four patients were referred by their providers based on clinical symptoms. The time period between the initial diabetes diagnosis to confirmed diagnosis of MODY ranged from a few months to 41 years. Many patients ($n = 5$) received suboptimal treatment before their MODY diagnosis.

3.3 | Barriers and facilitators to a MODY diagnosis

Extracted barriers and facilitators were grouped into three overarching themes: patient-, provider-, and healthcare system-level factors (Table 2).

3.3.1 | Patient and disease factors

Barriers: The nature of MODY symptoms can increase diagnostic difficulty. One barrier complicating the diagnostic process is the overlapping symptoms between MODY and the more common T1D and T2D: ‘I guess the doctors didn’t look at the fact. Type 2 diabetes was written all over my medical record and [doctors] just assume that’ [P2]. There was frustration about the seemingly nonsensical symptoms: ‘I was very surprised because I was 20, very skinny, athletic, I did all kinds of dance’ [P4].

Diagnosis of MODY also appears to be dependent on individual patient awareness and knowledge of the utility of genetic testing. A correct diagnosis through genetic testing allows differentiation of MODY from T1D and T2D and can provide a definitive diagnosis of the exact MODY subtype present, which informs cascade screening and testing of family members and is fundamental to select the most appropriate treatment for patients. However, due to confusion related to the atypical diabetes symptoms and to the utility of genetic testing, some participants chose not to pursue genetic testing: ‘I didn’t know the value of knowing whether you had MODY 1 versus. MODY 2. I sort of assumed that all MODYs were the same’ [P6]. ‘At that point my hemoglobin A1c wasn’t like off-the-charts or anything, I wouldn’t need to be on medicine so it wasn’t really worth it to do the genetic testing myself’ [P7].

Facilitators: Although the complexity of such patient presentations creates a challenging environment for diagnosis, in many cases the inconsistent symptoms or unique features of family history triggered further investigation and facilitated the speed of diagnosis: ‘There must be something going on because I didn’t fit into any normal description of type 2 or type 1 diabetic people. I’m not fat, I’m not experiencing any symptoms, I don’t have any trouble with my body basically... Then I started to do my own research because I don’t think this makes sense to me’ [P10].

In addition, awareness of the benefits of genetic testing, whether medical or psychosocial, acted as a facilitator in the diagnosing process: ‘It just helps me to know what bucket I fit into... I feel like it makes me a better participant in my own healthcare because I can talk

with my care team about why and which medication' [P3]. 'I think it was like ease of mind and a positive confirmation' [P7].

Most patients indicated that they should have been more 'forceful', 'firmer', and 'proactive' in their communication with their doctors, especially when they had a lack of faith in doctors' abilities to manage their diabetes: 'I would have actually taken the papers into my physician's office and said "look, it's right here in black and white. I fit the profile for MODY, probably MODY GCK, but I need to know." I would have actually crossed that line of just seeking advice and would've given advice' [P1]. 'Instead of listening to them [doctors] saying Oh, it's a little elevated. You're okay. Watch your diet, whatever. I wish I would have been saying we need to find an answer to why this is happening and then I think they would have thought more outside-the-box' [P4]. Being proactive and persistent might facilitate the differential diagnosis. Sometimes a quicker diagnosis attributed to patients' own persistence: 'So my awareness was my own personal awakening, it had nothing to do with what the physicians told me'.

3.3.2 | Provider factors

Barriers: The most frequently identified barrier was provider awareness and knowledge of MODY. All participants had encountered doctors who did not recognize MODY and had little understanding of the diagnostic indicators: 'I would say number 1 [barrier] is ignorance from the medical community. They seem to want to put you in type 1 or type 2 and are unwilling to or are unknowledgeable enough to know how to consider anything else... My first endocrinologist told me that even if you had a MODY diagnosis I wouldn't know what to do with it so I'd have to treat you like a type 2 diabetic anyway' [P2]. Some patients reported a sense that their doctors had not taken their symptoms seriously, potentially due to the rarity of MODY: 'It's very frustrating because I've seen so many doctors and so many different states and not a single person besides my doctor up here thought it [my family history] was weird' [P4]. The lack of explanation led to feelings of anger and frustration: 'I'm expecting if you're a specialist in diabetes you should know about these MODY things exist right? Do you know what happened when I told her [my endocrinologist] I think I might be MODY, she opened up her laptop and googled MODY. I was like seriously? I was pretty upset. I felt really disrespected' [P10].

The lack of knowledge also extended into decisions regarding referrals and treatment options: 'I tried to get my own physician to give me a referral to an endocrinologist...She [primary care provider] said I didn't need an endocrinologist and I was definitely type 2 diabetic and she was comfortable treating that and basically shut every door' [P2]. Providers' reluctance to order genetic testing for MODY was apparent: 'Instead of genetic testing we decided that we would experiment with different types of drugs and keep testing my sugars either on a daily basis or every three months to see if it works because it just ended up being the more economical way to go' [P6].

Another recurrent theme that may impede diagnosis is provider communication. Patients indicated that providers did not respond to their implicit cues or attempts to discuss concerns, expressed negative attitudes toward their beliefs and expectations, and provided vague or ineffective explanations for their complaints: 'I realized my symptoms clearly

matched MODY2. So then I wrote to my physician and said, since diabetes is in at least three generations in my family. I've also had prediabetes since my 30s or 20s. I eat a very strict low glycemic, low sugar diet and I walk. Shouldn't my diabetes be under the word monogenic rather than type II? It would require a different class of drug or no drug at all. I was explaining this to her [physician] and she said I can save you the genetics referral and tell you that yes, type 2 diabetes is one of the most genetic based illnesses we know in short. We don't tailor individual treatment. You are doing a fabulous job through lifestyle. And she said I suggest again that you attend a class to learn about diabetes. And so at that point, I gave up' [P1]. An underlying problem may be that providers and patients often disagreed on symptom etiology, which may also have negative emotional consequences on the doctor-patient relationship. Many patients perceived their providers lacked empathy when addressing their concerns: 'I feel like it was very overwhelming and I feel like I didn't get the support that I needed. I felt like they treated me like I was some dumb 20 year old who didn't know what was going on' [P4].

Facilitators: Although most patients described waiting a long time and being delayed, some felt that their MODY diagnosis had been swift, primarily due to the quick-thinking actions of their doctors. 'My dad had known of high blood sugar running in the family... Immediately my physician asked me to do a family tree, and he asked what was their physical appearance or fitness as well. So from the combination of that information and if they had high blood sugar, he was able to suspect highly that I had MODY' [P6].

3.3.3 | Healthcare system factors

Barriers: The lack of insurance coverage for genetic testing was one major barrier to obtaining a diagnosis of MODY. Prior to joining the PDMP, most participants were aware of the existence of genetic testing. However, they did not pursue the testing partially due to the cost and lack of insurance coverage: 'they [insurance plan] refused to cover it because it was not a procedure that's done in the lab where I have a main network and that network just did not cover that test' [P9].

Some participants recalled challenges related to a proper and timely referral. Patients explained how that they had never accessed their endocrinologist initially: 'She [primary care provider] wouldn't refer me, she keeps saying that referral for the people that are really bad, like A1Cs that are around 10. But she said I'm free to self-refer and she gave me their phone number. However, when I called that number, a week or two before that they had discontinued taking self-referrals' [P1]. There are very few health facilities that could offer genetic testing for MODY, some patients found that distance and travel time to a knowledgeable provider was another barrier to diagnosis: 'The nearest one [health facility] is five hours away. So I wasn't going to go drive with my three kids five hours away to tell them something that may or may not happen' [P4].

Facilitators: From the patient's perspective, online patient resources and support groups were usually considered to be a facilitator to MODY diagnosis, with many patients describing interacting with other patients as a positive aspect of their journey. Patients described not noticing or acting upon their atypical diabetes symptoms until they were

influenced by other people: 'I joined a few diabetes Facebook groups and in those groups is what someone mentioned MODY' [P4]. Patients have also indicated that they would like more informational guidance: 'I'm just thrilled that with my simple Google searches of my symptoms I was able to find the term monogenic, but at that point, except for different studies that I found, like National Institute of Health website, I was pretty much shut out. I couldn't find the name of the lab that would test for this and I just got totally frustrated' [P1].

4 | DISCUSSION

This study provides an insight into patients' trajectory to receiving a genetic diagnosis of MODY, by demonstrating the range of barriers and facilitators to diagnosis. Patients in this study were found to have experienced significant diagnostic delays. Many patients visited several medical professionals, including endocrinologists, over a number of years, but MODY was not suspected. Patients were commonly misdiagnosed with T1D or T2D, followed by an extended period of being untreated or incorrectly treated. This caused many patients to suffer side effects of inappropriate medicines and left them with feelings of anger, frustration, and confusion.

We identified barriers and facilitators that are reflected in Anderson's model and similar to those found with the diagnosis of other conditions (Armstrong, Rochnia, Harries, Bundock, & Yorke, 2012; Murray, Toussaint, Althaus, & Lowe, 2016; Parsonage, Hiscock, Law, & Neal, 2017). Some factors, such as the overlapping symptoms with T1D or T2D, are inherent to the nature of MODY and cannot be changed. However, these factors need to be accounted for in future research and clinical practice. On the other hand, some barriers to MODY diagnosis are modifiable and warrant further investigations.

4.1 | Practice implications

In our study, a lack of awareness and knowledge of MODY by medical professionals emerged as a significant barrier on the path to a confirmed diagnosis. Our findings suggest that many providers were not aware of MODY and questioned the utility of genetic testing in guiding treatment for MODY. Because of the complicated genetic nature of diabetes and the lack of a standard clinical guideline on genetic screening and testing for MODY, few providers are prepared to evaluate patients for the possibility of a monogenic diabetes etiology. As an example, the lack of knowledge about MODY and uncertainty of the value of genetic testing were acknowledged by physicians in an interview study in Netherlands (van der Zwaag et al., 2015). A survey of 151 genetic counselors revealed that more than half of the counselors were unaware of monogenic diabetes. Additionally, out of those that did know about monogenic diabetes, about 40% had never ordered a diagnostic genetic testing for monogenic diabetes because they did not know it existed (Miller, 2009). To address this knowledge gap, more training efforts are needed to teach providers to correctly identify clinical features of MODY upon encountering patients with a personal or family history of diabetes. The national Genetic Diabetes Nurse project in UK has been successful in promoting awareness of monogenic diabetes among other health professionals (Rigter et al., 2014; Shepherd, Colclough, Ellard, & Hattersley, 2014).

Getting a timely referral to knowledgeable specialists was another notable barrier. Patients were often treated in primary care settings for their diabetes and needed provider referral to see an endocrinologist. Some patients in our study expressed frustration about the length of time that it took to be referred to a specialist. However, a lack of local health resources and insurance coverage were reported and further complicated matters. To date, we are only aware of four specialist centers in the United States specifically identifying themselves as diagnosing and treating patients with MODY (Kovler Diabetes Center at The University of Chicago, NorthShore Medical Group in Skokie, IL, Massachusetts General Hospital Diabetes Genetics Clinic, University of Maryland Center for Diabetes & Endocrinology). In order to move more rapidly toward our goal of reversing the 95% misdiagnosis of MODY, we need to identify novel entry points into the diagnostic pipeline. Evidence-based practice guidelines that outline a diagnostic pathway may assist other healthcare professionals (e.g., primary care providers, pediatricians, diabetes educators, genetic counselors, clinical geneticists) to increase initial suspicion of MODY and pursue specific investigative testing. Brief risk assessment tools, such as the online MODY calculator (Shields et al., 2012), have been developed to support genetic testing for MODY. In addition, genetic counselors are in a prime position to identify patients and families that may be at risk for MODY through targeted questions during a family history, so that appropriate referrals and genetic testing can be made. For example, our group developed a pedigree assessment tool to use patient clinical symptoms, family history, and teamwork among providers to guide genetic testing for specific forms of MODY (Stein, Maloney, & Pollin, 2014).

The findings also highlight the importance of patient online resources that may facilitate timely diagnosis. In the absence of a reasonable explanation by their healthcare providers, patients in our study were inclined to search the Internet for answers of their symptoms. Many patients requested further laboratory tests even when they already received a 'definite' T1D or T2D diagnosis. Such requests often acted as facilitators and prompted their providers to take further action. Patients often use online health information to get a second opinion on diagnosis or treatment. However, a recent website analysis revealed that the online educational resources for monogenic diabetes were limited and had a high readability level (Guan, Maloney, Roter, & Pollin, 2018). Efforts are needed to increase comprehension and usability of online information related to the screening and diagnosis of monogenic diabetes.

4.2 | Study limitations

Caution should be taken in interpreting this retrospective qualitative interview study. We provided an in-depth description of patients' perspectives of their journey obtaining a MODY diagnosis, across the spectrum from a few months to 41 years. Although patients had detailed description of their experiences, the interview data rely on patients' recall and may not always accurately reflect what really happened. Similar to other qualitative research, our findings are not externally generalizable. Most patients were recruited from PDMP, and only one patient was recruited via online posting. All participants were female. Thus, their views may not reflect those of other populations undergoing this journey. For example, it is possible that males have different perspectives regarding provider communication compared to females, and participants recruited from a general diabetes population may have different knowledge and perceptions of the utility of testing. Importantly, patients taking a proactive

approach to their health care and diagnosis appeared to be overrepresented in this sample, as might be expected among individuals choosing to be interviewed. While this is a limitation, it also underscores that even in these cases, a correct diagnosis was difficult to obtain. Less proactive and/or educated patients would be expected to experience an even longer wait time for a correct diagnosis.

4.3 | Research recommendations

Despite these limitations, the diverse range of barriers and facilitators reiterates the complexity of the MODY diagnostic process. Limited awareness and knowledge of MODY from healthcare professionals and patients themselves account for most diagnostic delays experienced by patients in this study. Risk assessment tools to guide genetic testing for MODY need to be explicitly empirically in diverse populations. Implementation of diagnostic pathway beyond the endocrinology specialty may expedite the process of correct diagnosis. To this goal, a systematic review and evidence-based guideline for identifying possible MODY cases is currently under development under the NSGC Practice Guidelines Committee. Efforts to promote awareness of MODY and expand exposure to screening and testing may result in quicker diagnosis and ensure the downstream benefits to proper treatment.

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Participant demographic and clinical characteristics

TABLE 1

Participant	Pre-MODY journey				Diabetes management providers	Misdiagnosed years	Who initiated referral to genetic testing	MODY type
	Age	Race	Initial diagnosis	Treatment				
P1	67	Caucasian	T2D, pre-diabetes	None	Primary care doctor	41	Self-referral	GCK-MODY
P2	42	Caucasian	T2D	Metformin, Jardiance	Primary care doctor, diabetes educator, endurance sports doctor, endocrinologist	3	Endocrinologist	HNF4A-MODY
P3	45	Caucasian	T2D, 'possible MODY'	Glyburide (a sulfonylurea), insulin	Endocrinologist	29	Self-referral	HNF1A-MODY
P4	28	Caucasian	T2D, gestational	Glyburide (a sulfonylurea), Metformin, insulin	Primary care doctor, certified midwife, OB/GYN, endocrinologist	7	Self-referral	GCK-MODY
P5 ^a (parent)	7	Caucasian	T1D	Insulin	Pediatric endocrinologist	2	Self-referral	INS-MODY
P6	24	Caucasian	pre-diabetes, T2D	Sulphonylureas	Endocrinologist	2	Endocrinologist	GCK-MODY
P7	27	Caucasian	Pre-diabetes	None	Endocrinologist	1	Endocrinologist	GCK-MODY
P8	54	African American	T2D	Metformin, Januvia	Primary care doctor, endocrinologist	7	Endocrinologist	GCK-MODY
P9	31	Caucasian	Pre-diabetes	None	Primary care doctor, Endocrinologist	9	Endocrinologist	GCK-MODY
P10	27	Asian	T2D	Metformin	Primary care doctor, endocrinologist	<1	Endocrinologist	GCK-MODY

^aDemographic and clinical data are presented for the patient.

TABLE 2

Barriers and facilitators to genetic diagnosis of MODY

	Barriers		Facilitators	
	Main Findings	IDs	Main findings	IDs
Patient level	Nature of MODY symptoms (overlapping symptoms or family history features with T1D/T2D)	P2, P4, P9	Nature of MODY symptoms (inconsistent symptoms or family history features with T1D/T2D)	P1, P5, P10
	Perceived test utility (not aware of/misunderstand genetic testing utility)	P2, P3, P6, P7, P10	Perceived test utility (guide treatment, learn risk for family members)	P2, P3, P5, P6, P10
Provider level	Individual personality (not being more 'proactive', 'forceful', 'firm')	P1, P2, P3, P4, P5, P8, P10		
	Low provider awareness and knowledge	P1, P2, P3, P4, P5, P6, P7, P8, P9, P10	Knowledgeable providers	P6, P7, P10
	Provider communication (did not respond to patients' concerns, rushed discussions, vague explanations, lack of lack of empathy)	P1, P2, P3, P4, P8, P9, P10		
Healthcare system level	Cost of testing (limited insurance coverage, high out of pocket cost)	P2, P3, P5, P6, P8, P9	Patient resources (online search, patient support groups)	P1, P3, P4, P5, P10
	Access to knowledgeable providers (limited resources, difficult to get referrals)	P1, P2, P3, P4, P10		