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Research Article

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Personalized Medicine

Cost–effectiveness of genetic-based screening strategies for maturity-onset diabetes of the young

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Maturity-onset diabetes of the young (MODY) is often misdiagnosed as Type I or II diabetes. This study was designed to assess the cost–effectiveness of MODY screening strategies in Hungary, which included a recent genetic test compared with no routine screening for MODY. A simulation model that combined a decision tree and an individual-level Markov model was constructed to assess the costs per quality-adjusted life year of screening strategies. Stratifying patients based on age and insulin treatment followed by a risk assessment questionnaire, a laboratory test and genetic testing was the most cost-effective strategy, saving EUR 12 and generating 0.0047 quality-adjusted life years gained per screened patient. This screening strategy could be considered for reimbursement, especially in countries with limited resources.

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Maturity-onset diabetes of the young (MODY) is a heterogeneous group of disorders usually resulting in beta-cell dysfunction [1,2]. This form of diabetes is usually nonketotic, and most patients do not have pancreatic autoantibodies. The prevalence of MODY varies by country and ethnic group. In Europe, it is estimated to be 1–5 per 10,000 people, accounting for 1–5% of all diabetes mellitus (DM) cases. The UK, Norway, the Netherlands, Germany and Poland have comparable data on subtype distribution [3,4]. The most common subtypes are *HNF1A*-MODY, *GCK*-MODY and *HNF4A*-MODY. A recent genetic survey in Hungary found that in 89 MODY cases, *GCK* genes accounted for 73.0% of the cases, *HNF1A* accounted for 19.1 and 7.9% were attributable to other MODY-causing genes [5,6].

Based on patients' medical history and clinical characteristics, it is difficult to distinguish MODY from Type 1 and Type 2 diabetes. However, some signs and symptoms (i.e., lack of acute presentation, no ketoacidosis, no obesity and insulin resistance) indicate a higher probability [7]. Laboratory tests provide a further indication of the presence of MODY. Normal C-peptide levels and missing beta-cell autoantibodies are strong evidence against Type 1 DM. Previous studies have reported that autoantibodies are present in 82% of patients with Type 1 DM, hence the presence of autoantibodies against islet cell antigens suggests an autoimmune etiology (in Type 1 DM, especially in its early phase). Autoantibody tests can become negative in later phases of diabetes and have been reported to be positive in about 1% of MODY patients [8].

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As MODY is often misdiagnosed as Type 1 or Type 2 DM, these patients usually receive multiple oral and injectable antidiabetics, which may result in suboptimal glycemic control [9,10], loss of quality of life [11] and excess treatment costs. The definite diagnosis of MODY can be established by genetic testing. Several genetic test techniques can be applied such as Sanger sequencing or targeted next-generation sequencing. The latter enables massively parallel sequencing of dozens of genes that may play a role in the pathogenesis.

A number of predefined criteria have been reported to help physicians in making decisions about the initiation of genetic testing [2,12–14], including a freely accessible online risk assessment calculator [15]. The MODY calculator developed by Shields *et al.* collects data on patients' current age, age at the time of DM diagnosis, current treatment, time to insulin treatment, BMI, HbA1c levels, parents' DM history, ethnicity and information on the presence of some other pathologies. The test determines the probability of MODY and also suggests whether C-peptide and autoantibody tests should be performed. The validation of the calculator showed that 40% was the optimal probability cutoff that maximized both sensitivity (87%) and specificity (88%) in discriminating Type 1 DM and MODY patients [15].

The accurate diagnosis of MODY allows for changes in treatment in three subtypes. In most cases, pharmacological treatment is not needed for *GCK*-MODY patients, although a low glycemic index diet may be recommended, while *HNF1A*-MODY and *HNF4A*-MODY patients are able to maintain optimal glycemic control with sulfonylureas rather than insulin [16]. So, for these subtypes, diagnosing MODY will modify the pathway of care, lower or completely eliminate the treatment burden on individuals (releasing them from injectable treatment) and decrease the cost burden both on individuals and society. To date, only a few studies have investigated the cost–effectiveness of MODY screening [17–20]. These studies showed that genetic testing of a carefully selected DM population (e.g., young, 25–40-year-old patients) has good potential to be a cost-effective intervention in high-income countries [19]. In this study, the cost–effectiveness of diagnosing MODY patients with genetic testing in an Eastern-European population, Hungary, compared with the current diagnostic approach, which does not involve routine MODY diagnosis, was assessed.

Methods

Target population

A health economic model was developed to evaluate the cost–effectiveness of diagnosing MODY patients with genetic testing versus not routinely diagnosing MODY patients. The target screening population was patients with diabetes under 35 years of age who receive insulin treatment. To identify MODY, two patient stratification strategies were followed. In screening strategy 1, patients were first categorized with the MODY calculator, then high-risk patients were tested with massively parallel sequencing for MODY mutations (Figure 1A). In screening strategy 2, patients were first categorized with the MODY calculator, then high-risk patients were tested with the presence of autoantibodies against islet cell antigens, followed by massively parallel sequencing for MODY mutations of autoantibody-negative patients (Figure 1B).

Screening strategy 1 was deemed to reduce the number of tested patients to a manageable number while screening strategy 2 further reduced the number of patients, especially those assigned to expensive genetic testing. Differences in costs and health outcomes of the appropriately diagnosed and undiagnosed MODY patients were expected due to the following factors:

1. Diagnosed MODY patients with adequate treatment can have better glycemic control and fewer complications.
2. MODY patients on unnecessary insulin treatment can have more major hypoglycemic events.
3. Stopping unnecessary insulin treatment significantly reduces diabetic treatment costs as insulin is more expensive than sulfonylurea or diet.
4. Releasing patients from unnecessary use of insulin can significantly improve health-related quality of life (the detailed justifications of these factors are presented in the description of the submodels; see Supplementary Materials).

The cohort of detected MODY patients was calculated from the population data of a German registry, but the distribution of the simulated cohorts, *HNF1A* (62.18%), *GCK* (29.18%) and *HNF4A* (8.64%) MODY patients, were calculated based only on the insulin-treated patients in this German registry [21]. In addition, the male/female ratio (males: 39.16%) and age (mean age: 20.93 years) were adopted from this registry.

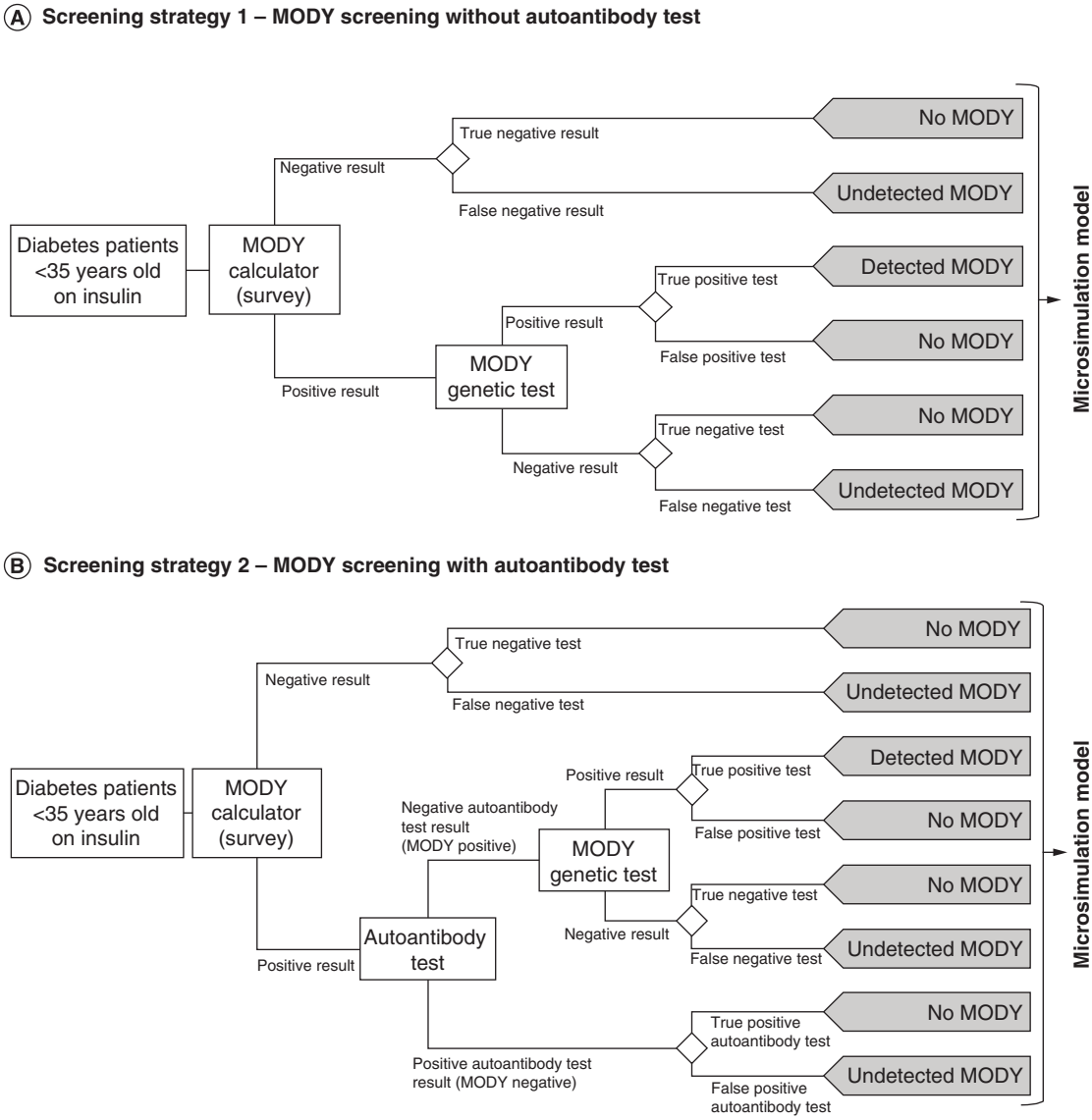

Figure 1. Decision tree for screening for maturity-onset diabetes of the young. (A) Screening strategy 1: MODY screening without autoantibody test. **(B)** Screening strategy 2: MODY screening with autoantibody test. As the model assumes 0% probability for false-negative and false-positive results from genetic testing, these branches are not containing any patients in the model. The options are still shown in this figure to consider all potential patient routes. MODY: Maturity-onset diabetes of the young.

Model structure

The cost–effectiveness model included two main modules: a decision tree representing the screening strategies and a patient-level Markov simulation model estimating the long-term effects of therapy changes in detected MODY patients compared with no change in therapy in non-MODY patients.

The decision tree module takes individuals through the patient stratification process, after which untested patients and patients with negative genetic tests remain on their original treatment. Patients with positive genetic tests change their therapy so that *GCK*-MODY patients switch to no treatment, while *HNF1A*- and *HNF4A*-MODY patients switch from insulin to sulfonylurea treatment.

The Markov simulation module was based on the Type 2 DM model published by Nagy *et al.* [22]. The Type 2 DM model was adapted to MODY and considered six diabetic complications that were simulated through a series of Markov submodels and corresponding health states (Figure 2). Complications were hypoglycemia, neuropathy, foot ulcer, retinopathy, macular edema and nephropathy. The simulation technique allowed patients to simultaneously

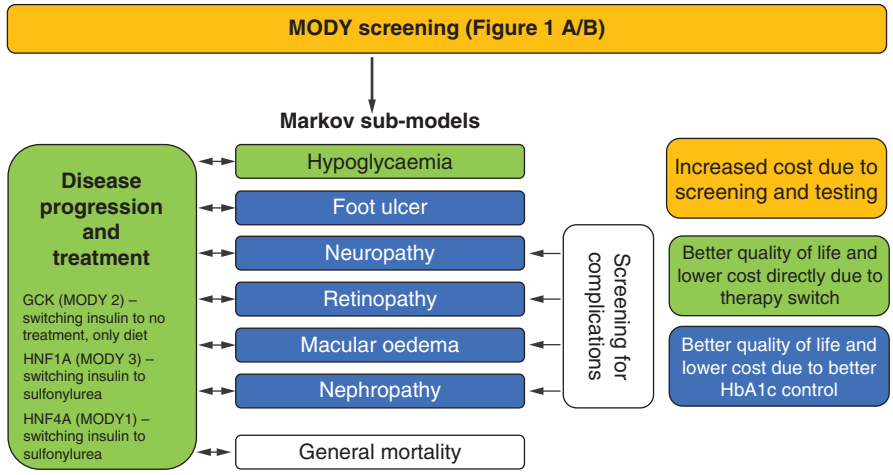

Figure 2. Structure of diabetes disease progression model with submodels.
MODY: Maturity-onset diabetes of the young.

stay in multiple submodels, thereby allowing patients to develop multiple complications within each Markov cycle and over the simulation period. The submodels are interconnected: progression in one complication has the potential to influence progression in other complications. A detailed description of the submodels is provided in Appendix 1 (in the Supplementary material).

Model parameters & inputs

The cutoff value for the MODY calculator above which patients were assigned to the high-risk group was 40%, which corresponded to the best combination of sensitivity and specificity (i.e., 87 and 88%, respectively) [15]. The probability of false-negative and false-positive results of genetic testing was set at 0.0% (i.e., both sensitivity and specificity of the genetic testing were assumed to be 100%). Based on McDonald *et al.,* less than 1% (5/508) of MODY patients have positive autoantibody tests [8]. This proportion of patients remained undetected in screening strategy 2 (see patients with positive autoantibody test in Figure 1B). Full compliance with screening was considered as patients were assumed to have a strong incentive to improve their quality of life by ending insulin therapy.

Physiological parameters for *GCK*-MODY patients were assumed to progress similarly to those of the general population. *HNF1A*- and *HNF4A*-MODY patients progressed similarly to patients with Type 1 DM. After the successful switch to sulfonylurea, an instant 0.9% reduction in HbA1c level was assumed based on literature data [9,10].

The progression of disease parameters (transition probabilities) in the submodels are described in Appendix 1. Sources of input data are published literature (articles on randomized clinical trials and observational studies) and expert opinion in cases where data were not available.

Country-specific general mortality data were taken from the Hungarian Central Statistics Office database [23]. Age- and gender-specific general utility data were derived from the national health survey by Boros *et al.* [24]. Diabetes complication-related disutility values were derived from the international literature and adjusted with general age- and gender-specific utilities (see Appendix 1). It was assumed that the genetic test had no negative effects on patients' quality of life.

The costs of autoantibody lab tests and the cost of completing the MODY questionnaire were calculated using tariffs of the National Health Insurance Fund (NHIF) in Hungary [25]. The costs of complications (including costs of screening where relevant) were calculated based on the inpatient and outpatient care tariffs of the NHIF [25]. Due to a lack of local data, the cost of a genetic test panel was derived from the publicly available price in the UK (diabetesgenes.org) and converted to Hungarian forints (HUF) using the average exchange rate in 2021 [26]. The results of the model were converted to euros (EUR) based on the average EUR/HUF exchange rate in 2021 (1 EUR = 358.52 HUF) [26]. The analysis was performed from a third-party payer perspective considering the direct medical costs of the NHIF.

Table 1. General input parameters.

Parameter	Value	Ref.
Discount rates		
Cost	0.037	[29]
QALY	0.037	
Costs, euros		
MODY questionnaire	2	[30]
Autoantibody test	4	[30]
MODY genetic test	716	[31]
Cost of HbA1c measure, outpatient	6.6	[30]
Insulin (daily)	0.86	[32]
Sulfonylurea (daily)	0.08	[32]
Health utility/disutility		
Insulin treatment-related disutility	0.0135	[11]
Other inputs		
Assumed prevalence of MODY	0.007	[15]
MODY questionnaire cutoff	40%	
MODY questionnaire sensitivity	87%	
MODY questionnaire specificity	88%	
Autoantibody test, MODY probability if positive	0.99%	[8]
Autoantibody test, T1DM probability if positive	82.0%	
0-GCK is simulated like *1A 4A*, *1-GCK* patients have no additional complications related to HbA1C without treatment	1	expert opinion
Hb1Ac decrease when newly diagnosed MODY patient is switched from insulin to adequate treatment (sulfonylurea or no treatment), %	0.9	[9,10]
Model time horizon, years	20	
Year calculation for daily costs, days	365, 25	
Number of cycles in a year	4	
Optional screening input in cycles, vision	4	expert opinion
Optional screening input in cycles, neuropathy	4	
Optional screening input in cycles, nephropathy	4	
Diet for *GCK* MODY patients	0	
HbA1c control multiplier for insulin	1	expert opinion
HbA1c control multiplier for *1A*/*4A* patient treated with sulfonylurea	0.25	
HbA1c control multiplier for *GCK* patient treated without treatment	0	

HbA1c: Hemoglobin A1c; MODY: Maturity-onset diabetes of the young; QALY: Quality adjusted life year; T1DM: Type 1 diabetes mellitus.

Sensitivity analyses

Scenario analyses were performed to explore the impact of using different cutoff points for the MODY questionnaire. One-way deterministic sensitivity analysis was performed including the input parameters of the initial screening and testing decision tree. Probabilistic sensitivity analysis (PSA) was conducted with 1000 iterations with all input parameters (for both parts of the model) including expert judgment. The input parameters are detailed in Table 1. The results of the PSA are presented on a cost–effectiveness plane and on cost–effectiveness acceptability curves.

Model outcomes

The cost–effectiveness model reports the costs and quality-adjusted life years (QALY) of the simulated cohorts and the ratio of their differences (incremental cost–effectiveness ratio [ICER]). The model also provides the differences in complications between undetected (insulin-treated) and detected (appropriately treated) MODY patients. The time horizon of the analysis was 20 years, and the length of the Markov cycles was 3 months. According to the Hungarian guideline for conducting health economic analyses, a 3.7% yearly rate was used to discount QALYs and costs, and the willingness-to-pay threshold for one QALY was set at 23,753 EUR/QALY, which is 1.5-times the Hungarian gross domestic product per capita [27] and in line with governmental guidance [28].

Table 2. Complication-related outcomes in base case scenario on 20-year time horizon.

	Insulin	Sulfonylurea or diet	Difference
Incidence of major hypoglycemic events/person-year (% of patients affected)	0.03 (48.63%)	0.00 (0.00%)	-0.03
Neuropathy-free survival in years (% of patients affected)	16.21 (32.85%)	19.89 (1.62%)	3.67
Ulcer-free survival in years (% of patients affected)	17.77 (21.50%)	18.26 (15.39%)	0.49
Retinopathy-free survival in years (% of patients affected)	11.79 (57.98%)	15.12 (38.85%)	3.33
Macular edema-free survival in years (% of patients affected)	18.04 (25.35%)	18.92 (14.52%)	0.87
Nephropathy-free survival in years (% of patients affected)	19.18 (7.10%)	19.48 (4.24%)	0.29
Overall survival (% of patients died during 20 years)	19.88 (1.70%)	19.89 (1.62%)	0.01

Table 3. Results of the base-case analyses.

	Cost (EUR)	QALY†	Delta cost† vs no screening (EUR)	Delta QALY† vs no screening	ICER
No screening	7362	12.1488			
MODY screening with autoantibody test (screening strategy 2)	7349	12.1535	-12	0.0047	Dominant
MODY screening without autoantibody test (screening strategy 1)	7419	12.1536	57	0.0048	11,993

†Discounted values.
EUR: Euro; ICER: Incremental cost–effectiveness ratio; MODY: Maturity-onset diabetes of the young; QALY: Quality adjusted life year; T1DM: Type 1 diabetes mellitus.

Results

Complication-specific events

The model shows that diagnosing MODY patients and switching their therapy from insulin to low-dose sulfonylurea (for *HNF1A*- and *HNF4A*-MODY patients) improves disease-free survival for five complications of diabetes: neuropathy, ulcer, retinopathy, macular edema and nephropathy. As an example, on a 20-year-long time horizon, the model results show that due to therapy switch neuropathy appears 3.67 years later on average, which could be a meaningful improvement for MODY patients. Therapy switch also cancels out major hypoglycemic events (for all MODY types) and improves patients' overall survival. Table 2 summarizes the complication-related outcomes during the 20-year time horizon, and switching treatment showed improvement in average complication-free survival and in the number of patients affected by each complication.

Base-case cost–effectiveness analyses

Patients without screening are expected to cost EUR 7362 and accrue 12.1488 QALYs over 20 years (Table 3). Patients with MODY screening are expected to cost EUR 7419 in screening strategy 1 and EUR 7349 in screening strategy 2 without and with autoantibody test, respectively, while they will accrue 12.1536 QALYs in screening strategy 1 and 12.1535 QALYs in screening strategy 2 over 20 years, respectively. MODY screening without an autoantibody test is considered cost-effective (screening strategy 1 ICER: 11,993 EUR/QALY) compared with no screening. Screening strategy 2 results in 12.1535 QALYs gained and EUR 7349 cost accrued, which clearly dominates the no-screening strategy. Screening strategy 1 compared with screening strategy 2 accumulates 0.000047 QALYs with an additional EUR 69 (ICER: 1,466,885 EUR/QALY), which cannot be considered cost-effective. Screening strategy 2 generates slightly fewer QALYs because of patients with a false-positive autoantibody tests.

Sensitivity analyses

Scenario analyses for the cutoff points showed that increasing the cutoff points of the MODY calculator (increasing specificity and decreasing sensitivity) decreases the cost of each identified MODY patient, leading to lower ICERs in both screening strategies (see Appendix 2 in the Supplementary Material). The one-way sensitivity analysis showed that the accuracy of the screening sessions before genetic testing had the biggest impact on the ICER. Figure 3 shows the impact of changing the screening-related parameters by 10% in screening strategy 2. It is important to note that varying the parameters did not change the conclusion related to screening strategy 2, that is, screening strategy 2 is dominant over no screening and screening strategy 1.

The results of the probabilistic sensitivity analysis are presented in Figure 4. All runs of the model provided QALY gains, while costs showed more variety, and there were results both in the positive and negative quadrants.

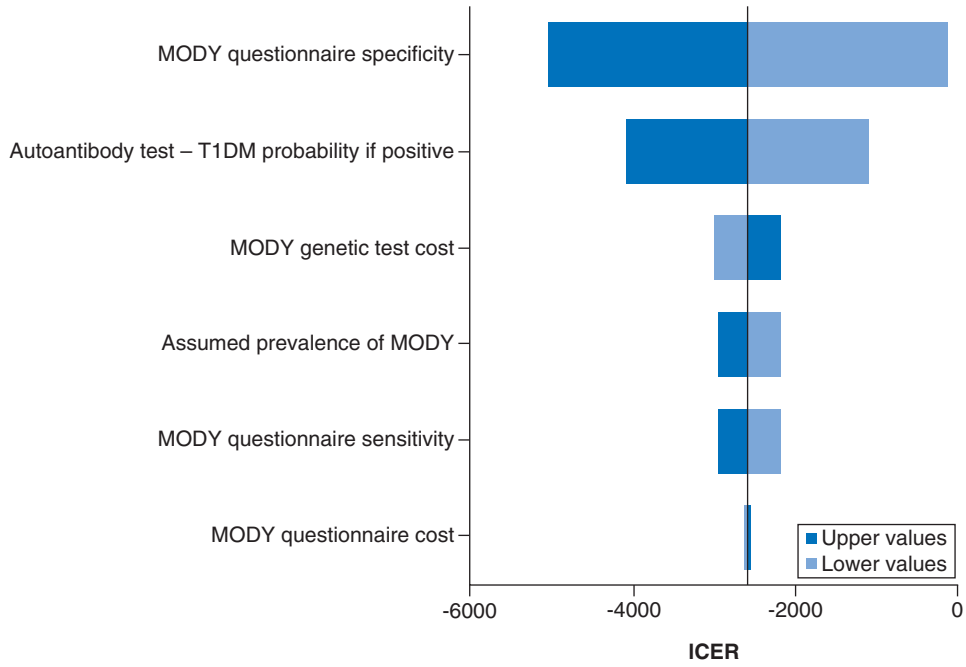

Figure 3. Tornado diagram of deterministic sensitivity analysis of screening strategy 2.
ICER: Incremental cost–effectiveness ratio; MODY: Maturity-onset diabetes of the young; T1DM: Type 1 diabetes mellitus.

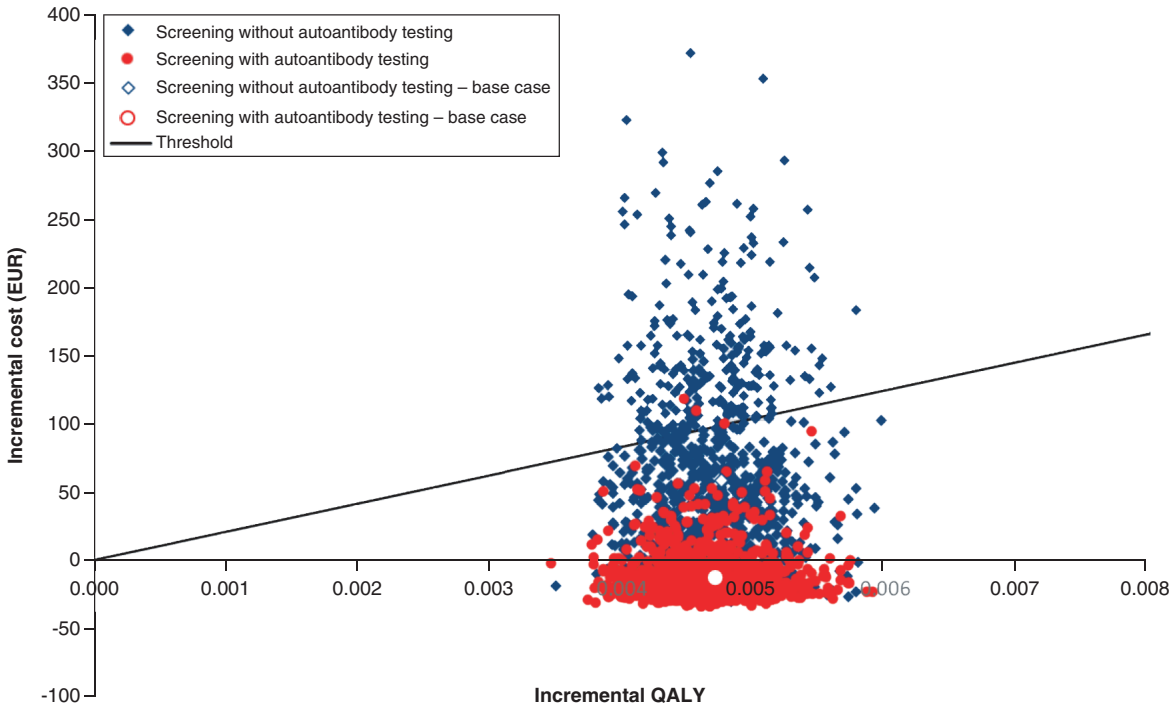

Figure 4. Scatter plot results of probabilistic sensitivity analysis on a cost–effectiveness plane.
Incremental quality-adjusted life years and costs are compared with no screening for maturity-onset diabetes of the young.
EUR: Euro; QALY: Quality adjusted life year.

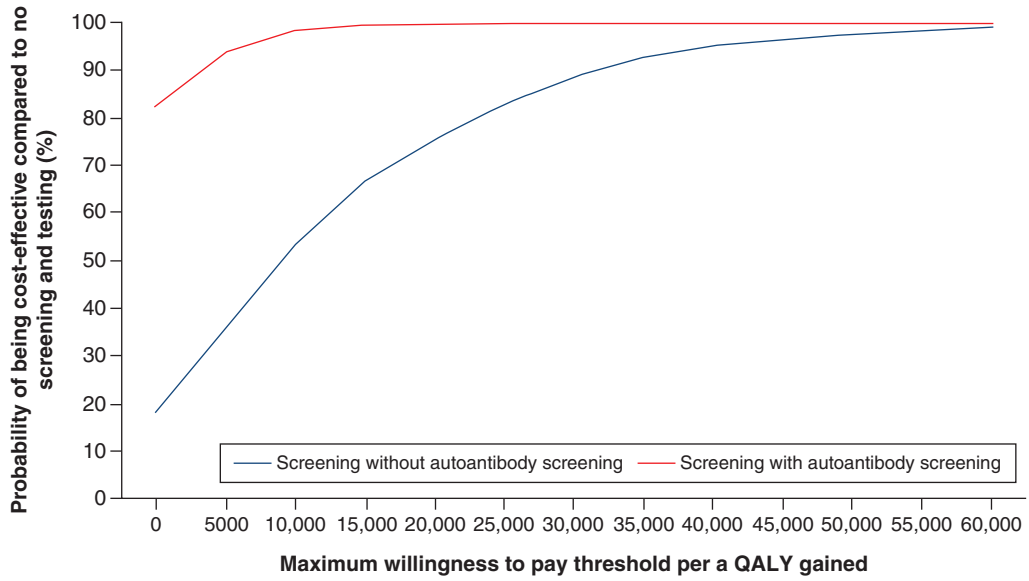

Figure 5. Cost–effectiveness acceptability curves of two alternative screening strategies (screening strategies 1 and 2) compared with no screening.
QALY: Quality adjusted life year.

The cost–effectiveness acceptability curves show that, applying a 23,753 EUR/QALY willingness-to-pay threshold, in screening strategy 1 there is a 76% probability that diagnosis without autoantibody laboratory test is cost-effective and there is an 18% probability of being dominant compared with no diagnosis (Figure 5). Screening strategy 2 has a 100% probability of being cost-effective and about 83% probability of being dominant over no detection.

Discussion

In this study, two screening strategies to diagnose MODY patients were compared with the current clinical practice of no routine screening of patients. High-risk patients were identified from the target group of insulin-treated diabetes patients under the age of 35 by applying a risk assessment questionnaire. These patients were then tested with next-generation sequencing. This multistep screening strategy was found cost-effective compared with no routine screening (i.e., QALY gains were achieved at acceptable costs). When autoantibody laboratory test was added to the diagnostic pathway, QALY gains were accompanied by cost savings, an even more attractive scenario for healthcare payers.

Direct comparison of our results to those of previous analyses [17–20] that assessed the cost–effectiveness of genetic screening for MODY is difficult. These analyses applied heterogenic methodology such as the included population (age, DM type), time horizon, applying or not prescreening with biomarkers, including or not the relatives of the probands to a genetic test. Consequently, the results of these analyses were also heterogenic showing genetic tests either not cost-effective [19,20] or dominant strategy [17,18] over the comparator.

QALY gains of the diagnosed patients were driven by switching from injectable insulin either to oral sulfonylurea for patients with *HNF1A*- and *HNF4A*-MODY mutations, or no treatment for patients with *GCK*-MODY mutation [11]. This can be expected to provide both emotional and physical relief and long-term reduction of diabetes (treatment)-related complications [9,10]. Due to annulling rare but life-threatening major hypoglycemic events that may occur due to insulin treatment, modest survival gains were achieved, too. Important differences in the frequency of long-term minor complications such as retinopathy and neuropathy and modest differences in major complications such as foot ulcer, macular edema and nephropathy were estimated. The patient stratification scenario with laboratory testing achieved slightly fewer QALY gains compared with the more expensive stratification process (no laboratory testing). This was due to the imprecision of the autoantibody test causing misdiagnosis in 1% of the patients with MODY (false negativity).

There was a noteworthy difference between the costs of the two screening strategies because of the difference in the number of patients who were assigned to genetic testing. In screening strategy 2, the autoantibody test

sufficiently reduced the population assigned to genetic testing (by excluding the autoantibody-positive Type 1 DM patients); to five-times fewer patients needed genetic testing. The proportion of patients who needed genetic testing made a massive difference in the average costs of screening and resulted in cost savings for the screening strategy using autoantibody laboratory tests. Finding the optimal patient stratification preceding expensive genetic testing was a game changer.

There were a few limitations in our analysis. Similarly to the original diabetes model [22], assumptions and simplifications related to the patient and treatment pathways were made, to keep the complex modeling exercise as plain and transparent as possible. These were reported in Appendix 1 and in the original paper by Nagy *et al.* [22]. Diagnosis of MODY with genetic testing is not part of the diabetes care protocol in Hungary. Hence, only a few local MODY-specific epidemiological, disease progression and outcome data were available, leading to literature- and expert-driven assumptions. Similarly, due to a lack of sufficient data, we could not allow for interdependence due to the sequential use of the MODY questionnaire, laboratory tests and genetic test results. The cohorts of detected MODY patients were defined based on German registry data [21]. Also, due to the lack of local data, the cost of genetic testing was based on UK cost data. Full compliance with genetic testing was considered as patients were assumed to have a strong incentive to improve their quality of life by changing their current insulin therapy. The model applied only a 20-year time horizon due to a lack of sufficient data on the long-term outcomes of MODY patients. The sensitivity and specificity of the screening tests in the submodels of some DM complications were considered perfect (i.e., 1.0) as the results of these tests defined the presence (or absence) of a complication in daily practice.

Some factors not considered in the analysis might further improve the cost–effectiveness of MODY genetic diagnosis. The impact of screening the relatives of diagnosed patients to detect the disease in an early stage was not analyzed, but could potentially provide further benefits to patients and impact healthcare spending. Identifying MODY in women under 35 years of age to prevent gestational and neonatal complications and inadequate antidiabetic treatment was not in the scope of the analysis. The analysis was performed from the perspective of the public payer; only direct medical costs were included, however, if the analysis had had a societal perspective, it could have captured additional benefits (e.g., labor market gains). Our analysis did not consider possible differences in the access to the infrastructure required for genetic testing across the country. Finally, our analysis was replicated in the context of two other health systems, The Netherlands and the UK and provided very similar results [33]. These results, taken together, provide a strong case to consider genetic testing to diagnose MODY patients in countries with a high prevalence of insulin-treated diabetes patients under the age of 35.

Conclusion

This analysis demonstrated that genetic testing to diagnose MODY patients in a well-defined, preselected, target population presents good value for money in the context of Hungarian healthcare. Consequently, this diagnostic approach could be considered for reimbursement, especially in countries with substantial financial constraints. Personalization of treatment with genetic testing covers a wide range of therapeutic areas, some of which significantly increase costs while others result in cost savings. This study draws attention to the potential benefits of personalization *via* well-designed patient stratification, resulting in cost savings and improved quality of life. It is important to find further personalization methods that have the potential to reduce the burden on healthcare systems.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/pme-2023-0023

Author contributions

G Kovács, D Nagy, L Szilberhorn and B Nagy initiated the research and developed the economic model. G Kovács, T Zelei, MR Mölken and B Nagy supported the development of the conceptual modeling framework. G Kovács, D Nagy and L Szilberhorn collected the model input parameters and ran the base case and scenario analyses. H Vellekoop, S Huygens and R Koleva-Kolarova

reviewed the model. G Kovács, L Szilberhorn, T Zelei and B Nagy interpreted the model results and developed the draft manuscript. H Vellekoop, S Huygens, M Versteegh, MR Mölken, R Koleva-Kolarova, S Wordsworth and A Tsiachristas reviewed and commented on the draft manuscript. G Kovács, T Zelei and B Nagy finalized the manuscript. All authors read and approved the current version of the manuscript.

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

G Kovács, D Nagy, L Szilberhorn, T Zelei, Z Gaál, H Vellekoop, S Huygens, M Versteegh, M Rutten-van Mölken, R Koleva-Kolarova, A Tsiachristas, S Wordsworth and B Nagy have no conflicts of interest that are directly relevant to the content of this article.

Data sharing statement

The datasets supporting the conclusions of this article are included in the main text and in its supplementary materials, including model description and input data with data sources. All other datasets used and analyzed in the current study are available from the corresponding author upon request.

Executive summary

- The cost–effectiveness of different hypothetical multistep maturity-onset diabetes of the young (MODY) screening strategies was assessed in Hungary.
- The target screening population was patients with diabetes under 35 years of age who receive insulin treatment.
- Two patient stratification strategies were followed. In screening strategy 1, patients were first categorized using the MODY calculator, then high-risk patients were tested with massively parallel sequencing for MODY mutations; in screening strategy 2, patients were first categorized using the MODY calculator, then high-risk patients were tested with the presence of autoantibodies against islet cell antigens, followed by massively parallel sequencing for MODY mutations of autoantibody negative patients. Both strategies were compared with no screening for MODY.
- A simulation model that combined a decision tree and an individual-level Markov model was constructed to assess the costs per quality-adjusted life years of each screening strategy.
- Stratifying patients based on age and insulin treatment followed by a risk assessment questionnaire, a laboratory test and genetic testing appeared to be the most cost-effective strategy by saving EUR 12 and generating 0.0047 quality-adjusted life years gained per screened patient.
- These results draw attention to the potential benefits of personalization *via* well-designed patient stratification, resulting in cost savings and improved quality of life.
- Multistep screening strategy for MODY patients could be considered for reimbursement, especially in countries with limited financial resources.

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