SCREENING FOR MATURITY ONSET DIABETES OF THE YOUNG

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 824997.

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MODY - MATURITY ONSET DIABETES OF THE YOUNG

- MODY is the most common form of monogenic diabetes, caused by 13 mutations
- Accounts for at least **1%-5%** of all diabetes cases
- Age of onset typically **<35 years**
- The three most common mutation types
  - Hepatocyte Nuclear Factor 1 Alpha (**HNF1A**)-MODY
  - Glucokinase (**GCK**)-MODY
  - Hepatocyte Nuclear Factor 4 Alpha (**HNF4A**)-MODY

95% of all monogenic diabetes patients

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WHY BOTHER WITH DIAGNOSIS?

- Most of MODY cases are **misdiagnosed** as type 1 or type 2 diabetes
- With proper diagnosis **no insuline** treatment is required
  - **Dietary intervention alone** is usually enough for GCK-MODY patients
  - HNF1A-MODY and HNF4A-MODY patients are able to maintain optimal glycaemic control with **sulphonylurea**
  - Correct determination of the MODY subtype informs decisions regarding appropriate treatment and prognosis

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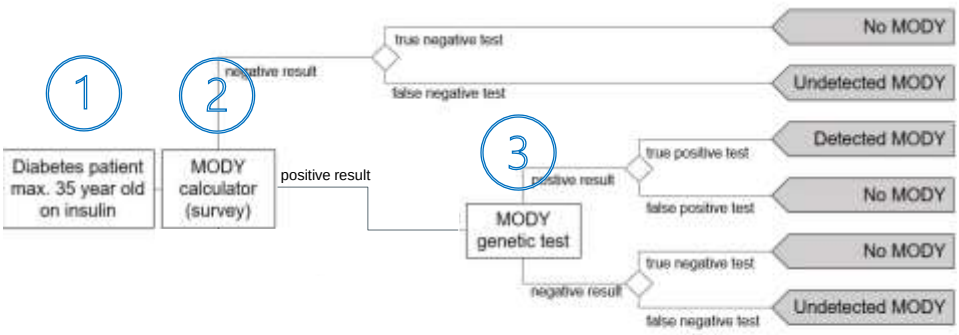
SCREENING FOR MODY PATIENTS - SCENARIO 1



MODY Probability Calculator

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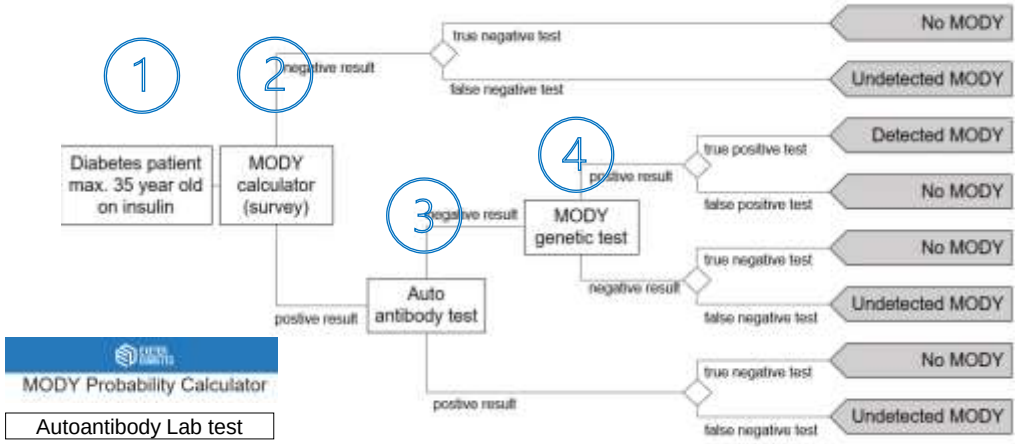
SCREENING FOR MODY PATIENTS - SCENARIO 2



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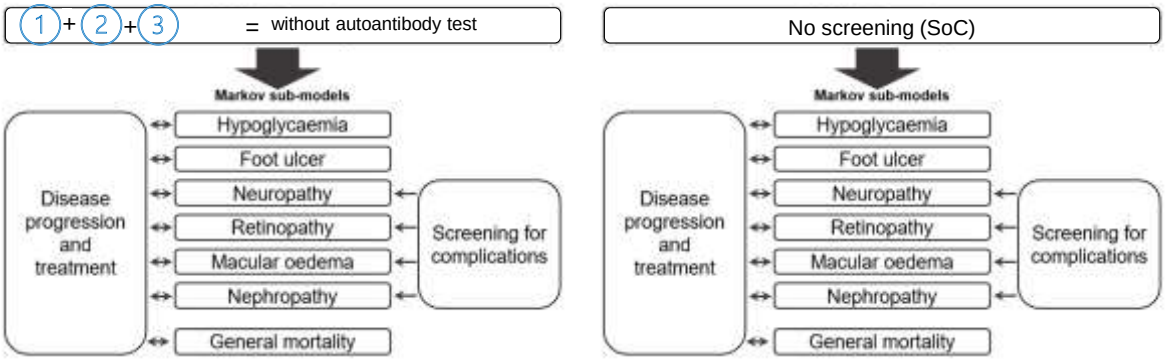
MODEL STRUCTURE

Scenario 1



Simulation model for diabetic complications and mortality: Nagy et al 2016

Time horizon: 20 years

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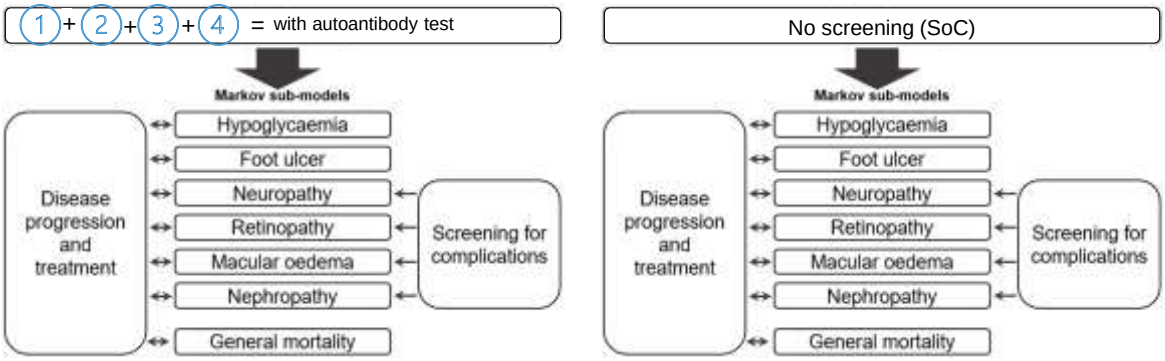
MODEL STRUCTURE

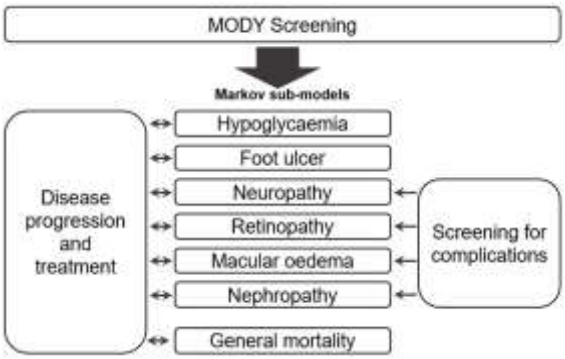
Scenario 2



Simulation model for diabetic complications and mortality: Nagy et al 2016

Time horizon: 20 years

CONSEQUENCES OF SCREENING



BOTH SCREENING STRATEGIES

- Less therapeutical costs + better quality of life
  - avoid hypoglycaemic events
  - less frequent complications (better HbA1c control)
- Extra costs of
  - genetic test: 730.9 EU
  - autoantibody test: 3.8 EU
  - MODY questionnaire: 2.0 EU

SCREENING WITH AUTOANTIBODY TEST

- 1% of patients is not detected

PRELIMINARY COST-EFFECTIVENESS RESULTS

	Cost (in €)	QALYs	Incremental Cost (in €)	Incremental QALYs	ICER
No screening	7,516	12.15			
MODY screening without autoantibody test	17,073	12.93	9,557	0.78	**12,244**
MODY screening with autoantibody test	5,455	12.93	-2,060	0.78	**dominant**

Threshold: 41,544

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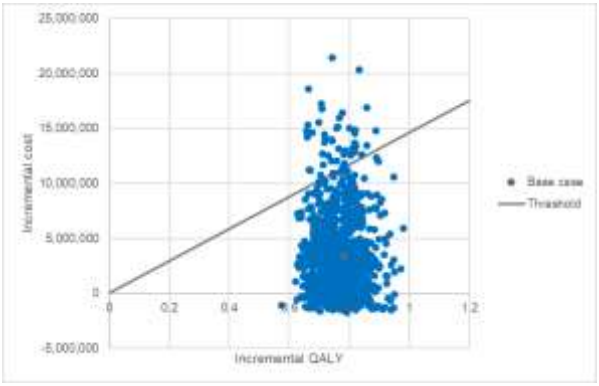
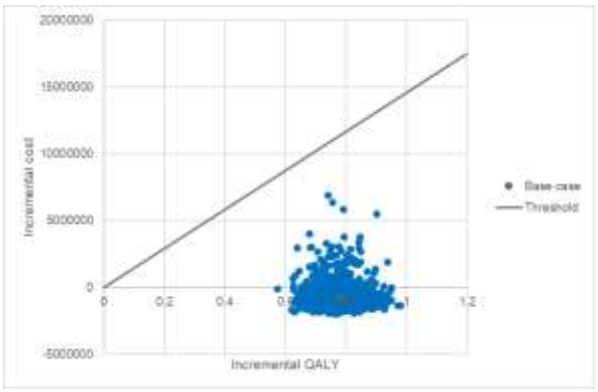
PROBABILISTIC SENSITIVITY ANALYSIS



SCREENING WITH GENETIC TEST ONLY



PRE-SCREEING WITH AUTOANTIBODY TEST + GENETIC TEST

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TESTING HECOPERMED RECOMMENDATIONS

14 of 23 recommendations were applied in our case study

- Our case study managed to address 15 out of 23 recommendations; 5 items were not applicable for our case, 4 items were not included.

	MODY
Addressed	14
Not applicable	5
Not included	4

Guidance items	Recommendations	Application to the MODY case study
Perspective and Discounting	1. For economic evaluations of PM, use the standard perspective as recommended by national HTA guidelines in the base case.	applied
	2. For economic evaluations of PM, use the standard discount rates as recommended by national HTA guidelines in the base case.	applied
Test-Treatment Pathways	3. Identify all relevant test-treatment pathways and justify why the pathways included in the model were selected.	applied
	4. When treatment requires the use of a test to stratify patients, include in the model the (downstream) costs and health outcomes of testing for both individuals who test (false-)positive and individuals who test (false)negative.	applied
	5. Ensure that the data used to estimate the diagnostic accuracy of a testing technology are appropriate to the patient population in the model.	applied
	6. When different cut-off values are in use to determine test results, clearly define the cut-off value assumed in the base case. Investigate the effect of alternative cut-off values on cost-effectiveness results using a sensitivity analysis.	applied
	7. When multiple tests are modelled in sequence, consider the interdependence between test results.	not included
	8. If there is a notable risk of increased morbidity or mortality as a result of waiting periods, incorporate in the model the costs and health outcomes due to the waiting periods.	not applicable
	9. Confirm that the assumed testing costs are accurate in the setting of interest and consider possible variations in costs across laboratories.	applied
	10. If relatives of index patients become eligible for genetic testing when the index patients test positive for a specific genetic marker, include the costs and health outcomes of testing relatives in the economic evaluation of the index patients.	not included
Effectiveness Data	11. Where possible, use effectiveness data from trials with two (or more) alternative treatment strategies.	applied
	12. When surrogate outcomes are used to estimate final outcomes, specify which data sources were used to estimate the relationship between surrogate and final outcomes and justify any assumptions made about the relationship	applied
	13. When the effectiveness of the comparator is estimated using external data, account for a possible time trend in the effectiveness.	not applicable
	14. When the effectiveness of the comparator for patients with a specific genetic marker is estimated using external data, account for the prognostic value of the genetic marker and differences in its prevalence across the different data sources.	not applicable
	15. Specify which data sources were used to estimate the association between the genetic marker(s) of interest and clinical outcomes and justify any assumptions made about the association.	applied
Extrapolating Survival	16. When extrapolating survival data beyond the study period, use expert opinion alongside statistical fit to choose the survival model.	not applicable
	17. When extrapolating survival data beyond the study period, account for any excess mortality and morbidity among long-term survivors.	not applicable
Additional Elements of Value	18. Only include elements of value recommended by national HTA guidelines in the base case. If additional elements of value are included in a sensitivity analysis, ensure possible elements of negative value are equally considered and included for both the intervention and the comparator.	applied
Incorporating Compliance	19. Include parameters reflecting patient and clinician compliance in economic evaluations for decision-makers who require cost-effectiveness results under realistic circumstances.	applied
	20. When including patient and clinician compliance in economic evaluations, confirm that the assumed compliance is accurate in the setting of interest and consider possible variation in compliance across societal groups.	not included
Uncertainty Analysis	21. When expert judgement is used to estimate values for the input parameters in the model, synthesise the elicited values into a probability distribution to be included in a sensitivity analysis.	applied
	22. Identify uncertainties in structural assumptions and decisions and investigate their impact on cost-effectiveness results through a sensitivity analysis. Parameterise structural aspects where possible.	applied
Managed Entry Agreements	23. If a managed entry agreement is being considered for intervention, including its conditions in the model evaluating the intervention.	not included

RECOMMENDATION 11

„Identify all relevant test-treatment pathways and justify why the pathways included in the model were selected."

- Inclusion of autoantibody testing is false negative in 1% of the MODY population
- We take the risk of loosing QALYs for 1% of patients but save costs
- IT WAS A GAME CHANGER

RECOMMENDATION 10

"Include the costs and health outcomes of testing relatives of index patients with inheritable genetic mutations in the model."

- Which relatives could have been included?
  - Siblings, easy to identify - **YES**
  - Parents, too old (>35) to switch original therapy - **NO**
  - Children – in a great distance of time to capture in a model - **NO**

POLLING QUESTION

Should it become common practice in cost-effectiveness models/analyses of personalized medicine to consider inexpensive patient stratification methods before the use of expensive diagnostics?