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Cost-Utility Analysis of Polygenic Risk Score in the Prevention of Type 2 Diabetes

Object-Oriented Individual-Level Model with Probabilistic Sensitivity Analysis (PSA)

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Background

- Type 2 diabetes (T2D) is a significant public health challenge.
- Obesity, unhealthy diet, and low physical activity are main risk factors of T2D, but genetic risk is also a factor in developing T2D.
- Recently, genomic-based polygenic risk scores (PRSs) have been suggested to improve the accuracy of risk prediction (**1**).
- The aim of this study was to assess the cost-utility of additional PRS testing (as a part of overall risk assessment) followed by a lifestyle intervention and an additional medical therapy when estimated 10-year overall risk for T2D exceeded 20% among individuals screened as high-risk based on traditional risk factors only.

Methods

- For a cost-utility analysis, a microsimulation state-transition model with PSA was constructed.
- Model parameters were estimated based on the national FINRISK follow-up study (n=15,868) and other real-world datasets. For example, parametric survival regression models were used to assess the baseline risk of T2D with and without genetic risk information.
- The model was built utilizing object-oriented programming paradigm: an object was created to represent every individual virtually. In turn, each individual was assigned into a cohort object (**Figure 1**). The model was written in R (**2**).
- Cost-effectiveness acceptability curve (CEAC) and the expected value of perfect information (EVPI) were also estimated. Cohort-level PSA was used in evaluating the impact of simultaneous variation in model parameters on the model results.

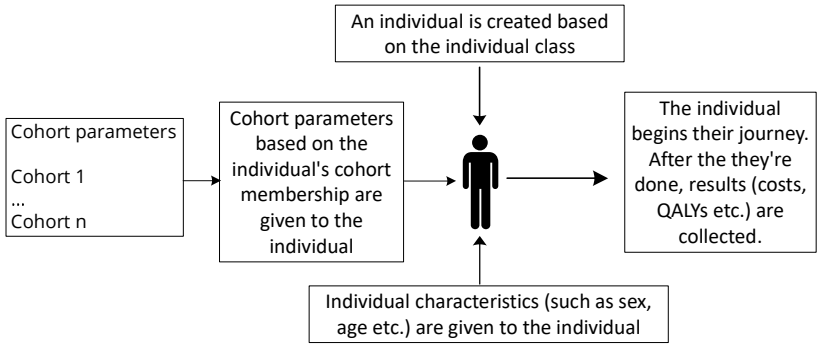

Figure 1. Overview of the object-oriented model structure

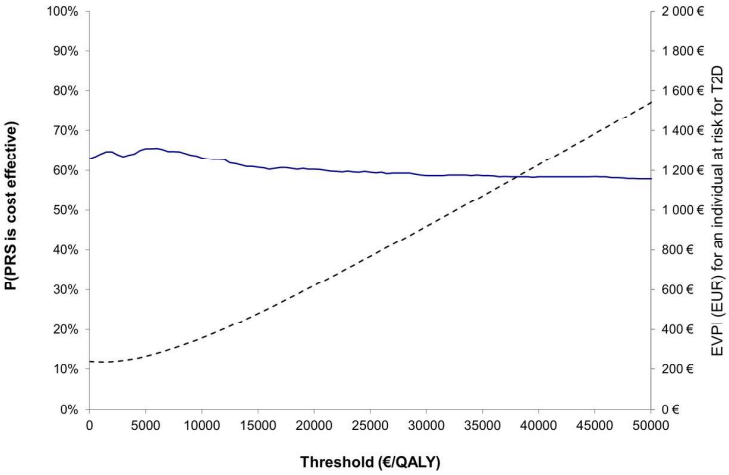

Figure 2. Cost-effectiveness acceptability curve (blue line; left y-axis) showing the probability that the PRS strategy is cost-effective compared to the usual practice, together with expected value of perfect information (dotted line; right y-axis) over a range of values for WTP

Results

- The use of targeted PRS strategy reclassified 12.4% of individuals as very high-risk individuals who would have been originally classified as high-risk.
- Over a lifetime horizon, the targeted PRS was the dominant strategy. The sensitivity analyses showed that PRS remained dominant in almost all simulations.
- However, there is still decision uncertainty since the probability of cost-effectiveness at a WTP of 0€/QALY was 63.0% (**Figure 2**). The corresponding EVPI estimate was 243€ per an individual.

Conclusions

- The results of the study (**3**) showed that PRS provides moderate additional value in risk screening leading to potential cost savings and better quality of life, comparing with the current T2D risk screening.

References:

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3) Martikainen J, Lehtimäki AV, Jalkanen K, Lavikainen P, Paajanen T, Marjonen H, Kristiansson K, Lindström J, Perola M. Economic evaluation of using polygenic risk score to guide risk screening and interventions for the prevention of type 2 diabetes in individuals with high overall baseline risk. Front Genet. 2022 Sep 15;13:880799.

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