Economic Evaluation of a New Polygenic Risk Score to Prevent Nephropathies in Type-2 Diabetic Patients

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INTRODUCTION

- The prevalence of diabetes is constantly increasing and currently affects 9.3% of the Canadian population. In 2025, it is projected that 12.1% of Canadians will be affected with diabetes, an estimated increase of 44% over 10 years.[1]
- One of the most prominent complications related to diabetes are renal problems. Approximately 50% of diabetic patients will develop some type of renal damage throughout their lifetime.[2]
- The most commonly reported renal complication in diabetes is diabetic nephropathy (DN). The current screening method for DN is based upon detection of albumin in the urine and decline of glomerular filtration rate, which occurs relatively late in the course of the disease.[2]
- Recently, we have genotyped 4,098 patients from the ADVANCE trial, a randomised controlled trial of blood pressure lowering and intensive glucose control in patients with type 2 diabetes (T2D), in order to build a polygenic risk score (PRS) for each of the renal and cardiovascular outcomes.[3,4]
- This study concluded that the risk for renal events was higher in patients with a high PRS and early onset diabetes.
- It was concluded that the implantation of the PRS as the main screening method for DN would result in an important clinical benefit and would potentially provide substantial cost savings for the health care system.

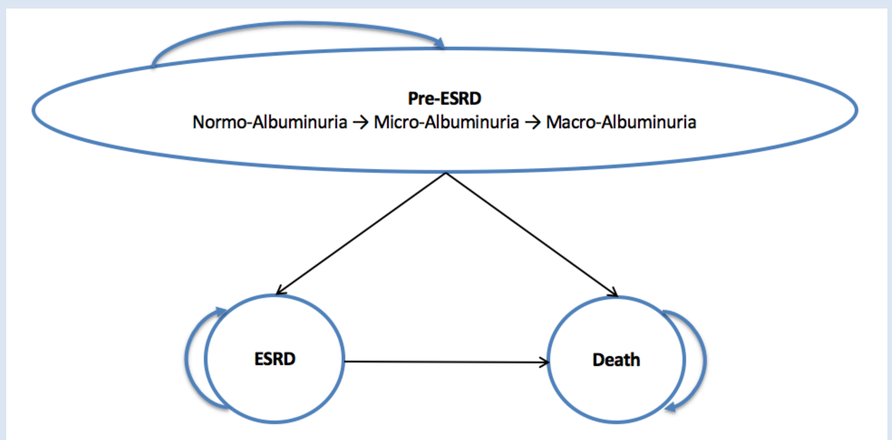
OBJECTIVE

- The aim of this study was to assess the economic impact of the implementation of the PRS for the prevention of DN in T2D patients, compared to usual screening methods, in Canada.

METHODS

- A cost-utility analysis was performed to assess the economic impact of a PRS for the prevention of DN in T2D patients, compared to usual screening methods (urinary ACR, serum creatinine, urine dipstick, etc.) [5]
- A Markov model was developed using 1-year cycles and a 5-year time-horizon.
- Markov health states were defined as: pre-end-stage renal disease (pre-ESRD), ESRD and death.

Figure 1. Markov Model Structure



- Model efficacy parameters were calculated based on prediction of outcome data by polygenic risk testing of the ADVANCE trial. Kaplan Meier curves were produced and extrapolated data was based on the best-fit curve using R software, fitted to parametric distributions. [6]
- In the base-case analysis, patients receiving the PRS and obtaining a high risk result were assumed to receive intensive glucose control treatment, while medium and low risk groups received standard glucose control treatment.
- Analyses were conducted from Canadian healthcare and societal perspectives.
- Cost data included: costs of screening for DN, drug acquisition costs, costs related to ESRD management and terminal care. The costs of productivity loss associated with ESRD were added from a societal perspective
- Results were expressed in terms of incremental cost per QALY gained.
- Scenario analyses were conducted using time-horizons of 10-years, lifetime and a 10-year time horizon using 9.5-year raw data.
- Deterministic and probabilistic sensitivity analyses (DSA;PSA) were conducted to assess the robustness of the results.

RESULTS

- **Base-Case Analysis:** the PRS compared to usual screening was associated with a decrease in cost (-$1,481 from a healthcare system perspective and -$1,803 from a societal perspective) and a QALY gain of 0.010. As a result, the ICUR of PRS versus usual screening over a 5-year time horizon was dominant, from both a healthcare system (Table 1) and societal perspective (Table 2)**.**

Table 1. Cost-Effectiveness Results – Base-Case Analysis Healthcare System Perspective

	Costs (CAD)	Δ Costs (CAD)	QALYs	Δ QALYs	ICUR
Deterministic					
Usual Screening	$5,815	-	4.25	-	-
PRS	$4,334	-$1,481	4.26	0.010	Dominant
Probabilistic median presented					
Usual Screening	$6,196	-	4.57	-	-
PRS	$4,572	-$1,625	4.58	0.010	Dominant

Table 2. Cost-Effectiveness Results – Base-Case Analysis Societal Perspective

	Costs (CAD)	Δ Costs (CAD)	QALYs	Δ QALYs	ICUR
Deterministic					
Usual Screening	$6,382	-	4.25	-	-
PRS	$4,580	-$1,803	4.26	0.010	Dominant
Probabilistic median presented					
Usual Screening	$6,804	-	4.57	-	-
PRS	$4,840	-$1,963	4.58	0.010	Dominant

Scenario Analysis

- **10-Year Time Horizon:** the PRS compared to usual screening was associated with a decrease in cost (-$2,711 from a healthcare system perspective and -$3,223 from a societal perspective) and a QALY gain of 0.054. As a result, the ICUR of PRS versus usual screening over a 10-year time horizon was dominant, from both a healthcare system and societal perspective.
- **Lifetime Horizon:** the PRS compared to usual screening was associated with a decrease in cost (-$2,924 from a healthcare system perspective and -$3,498 from a societal perspective) and a QALY gain of 0.126. As a result, the ICUR of PRS versus usual screening over a lifetime horizon was dominant, from both a healthcare system and societal perspective**.**
- **10-Year Time Horizon using 9.5 year data:** the PRS compared to usual screening was associated with a decrease in cost (-$3,013 from a healthcare system perspective and -$3,493 from a societal perspective) and a QALY gain of 0.045. As a result, the ICUR of PRS versus usual screening over a 10-year time horizon was dominant, from both a healthcare system and societal perspective**.**

Sensitivity Analysis

- According to the deterministic sensitivity analysis results, PRS remained a dominant alternative compared to usual screening in all analyses. Parameters that have the greatest impact on the base-case ICURs were the proportion of patients on dialysis, proportion of patients with in-center hemodialysis and the hazard ratio of ESRD related to high PRS.
- According to a willingness to pay threshold of $CA50,000/QALY, the PRS was a dominant alternative over the usual screening methods in 93.7% of the Monte Carlo simulations, from both a healthcare system and societal perspective.

CONSLUSIONS

- This economic evaluation suggest that, from a societal and Canadian health care system perspective, the PRS is a dominant option compared to usual screening methods, for the prevention of DN in patients with T2DM.
- The adoption of the PRS would not only be cost saving, but would also prevent ESRD and improve patients' lives.

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DISCLOSURES

- Kimberly Guinan is a masters student at the University of Montreal. She has received funding by the University as well as from the Canadian Association for Healthcare Reimbursement (CAHR).
- Jean Lachaine is the director and Catherine Beauchemin the co-director for Kimberly Guinan's masters project. Both are teachers at the University of Montreal.
- Pavel Hamet and Johanne Tremblay were responsible for the development of the clinical polygenic test. They both contributed as key opinion leaders in the model development.
- John Chalmers and Mark Woodward managed the ADVAMCE study. They have no conflicts of interest to declare.

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CAHR ACRSS The Canadian Association for Healthcare Reimbursement / L'association canadienne pour le remboursement des soins de santé