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Original Research

# The Long-Term Risks of End Stage Renal Disease and Mortality among First Nations and Non-First Nations People with Youth-Onset Diabetes

Roland F. Dyck MD<sup>a,b,\*</sup>, Ying Jiang MSc<sup>c</sup>, Nathaniel D. Osgood PhD<sup>b,d</sup><sup>a</sup> Department of Medicine, University of Saskatchewan, Saskatchewan, Canada<sup>b</sup> Department of Community Health and Epidemiology, University of Saskatchewan, Saskatchewan, Canada<sup>c</sup> Ontario Cancer Institute, Toronto, Ontario, Canada<sup>d</sup> Department of Computer Science, University of Saskatchewan, Saskatchewan, Canada

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## ABSTRACT

**Objective:** To compare the long-term risks of end stage renal disease and death among First Nations and non-First Nations people with youth-onset diabetes.**Methods:** Using Saskatchewan Ministry of Health administrative databases covering the period between 1980 and 2005, we conducted a retrospective cohort study of end stage renal disease and death among youth with diabetes diagnosed before age 20. We developed Fine and Gray sub-distribution hazards models and cumulative incidence functions for the 2 outcomes by First Nations status and duration of diabetes.**Results:** Incident cases of youth-onset diabetes were diagnosed in 352 First Nations and 2288 non-First Nations people. Mean ages at diabetes diagnoses were 11.7 and 11.2 years, respectively ( $p=0.13$ ). Adjusted for sex and age at diabetes diagnosis, the risk for end stage renal disease was 2.59 (95% CI, 1.11–6.04) times higher, and the risk for death 2.64 (95% CI, 1.44–4.87) times higher for First Nations compared to non-First Nations people. After 25 years, the cumulative incidence of end stage renal disease was 12.3% for First Nations people compared to 4.3% in their non-First Nations counterparts. Corresponding mortality rates were 14.6% and 7.2%, respectively.**Conclusions:** First Nations people with youth-onset diabetes experience higher long-term risks for end stage renal disease and death than their non-First Nations counterparts. Early identification of type 2 diabetes and secondary prevention of diabetic nephropathy are feasible short-term goals for this high-risk group. More effective primary prevention initiatives and programs to delay diabetes onset are imperative to reverse current trends.

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## R É S U M É

**Objectif :** Comparer les risques à long terme d'insuffisance rénale terminale et de mortalité des membres des Premières Nations et des non-membres des Premières Nations souffrant de diabète juvénile.**Méthodes :** À partir de la banque de données administratives du ministère de la Santé de la Saskatchewan couvrant la période de 1980 à 2005, nous avons réalisé une étude de cohorte rétrospective sur l'insuffisance rénale terminale et la mortalité des jeunes ayant reçu un diagnostic de diabète avant l'âge de 20 ans. Nous avons développé des modèles à risques en sous-distribution de Fine et Gray et les fonctions d'incidence cumulée de 2 critères de jugement selon le statut auprès des Premières Nations et la durée du diabète.**Résultats :** Les nouveaux cas de diabète juvénile ont été diagnostiqués chez 352 membres des Premières Nations et 2288 non-membres des Premières Nations. L'âge moyen lors du diagnostic de diabète était respectivement de 11,7 ans et de 11,2 ans ( $p = 0,13$ ). Ajusté selon le sexe et l'âge lors du diagnostic de

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Ying Jiang is currently with the Ontario Cancer Institute, but her work on this project stems from her position as a graduate student at the University of Saskatchewan.

\* Address for correspondence: Roland F. Dyck, MD, Department of Medicine, Royal University Hospital, 103 Hospital Drive, Saskatoon, Saskatchewan S7N 0W0, Canada.

E-mail address: [roland.dyck@usask.ca](mailto:roland.dyck@usask.ca)

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diabète, le risque d'insuffisance rénale terminale était 2,59 (IC à 95 %, 1,11–6,04) fois plus élevé et le risque de mortalité était 2,64 (IC à 95 %, 1,44–4,87) fois plus élevé chez les membres des Premières Nations que chez les non-membres. Après l'âge de 25 ans, l'incidence cumulée de l'insuffisance rénale terminale était de 12,3 % chez les membres des Premières Nations et de 4,3 % chez leurs homologues non-membres des Premières Nations. Les taux correspondants de mortalité étaient respectivement de 14,6 % et de 7,2 %.

**Conclusions :** Les membres des Premières Nations souffrant de diabète juvénile connaissent des risques à long terme plus élevés d'insuffisance rénale terminale et de mortalité que leurs homologues non-membres des Premières Nations. Le dépistage précoce du diabète de type 2 et la prévention secondaire de la néphropathie diabétique font partie des objectifs réalisables à court terme pour ce groupe exposé à un risque élevé. Des initiatives et des programmes de prévention primaire plus efficaces pour retarder l'apparition du diabète sont impératifs pour inverser les tendances actuelles.

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## Introduction

Indigenous peoples are experiencing a global epidemic of type 2 diabetes (1) and its complications (2), but most studies describing this pandemic have been conducted among adults. In Canada, however, a significant body of research on youth-onset type 2 diabetes stems from investigations carried out among First Nations people in Manitoba. Investigators there have shown that this population exhibits elevated rates of youth-onset type 2 diabetes (3,4), that a large proportion of affected individuals have been exposed to a diabetic intrauterine environment (5) and that early renal disease manifested by microalbuminuria is common (6). However, there is little information from Canada and elsewhere about the long-term risks for kidney failure and death among those with youth-onset diabetes or possible ethnic-based disparities in these devastating outcomes.

We recently published a population-based study that examined the epidemiology of diabetes among First Nations and non-First Nations youth in Saskatchewan from 1980 to 2005 (7). Although unable to distinguish between type 1 and type 2 diabetes, we showed that diabetes prevalence more than tripled among First Nations youth over the 25-year period while less than doubling among non-First Nations youth. The purpose of this follow-up research was to study the long-term risks of end stage renal disease and death in this cohort with youth-onset diabetes, and to determine whether those adverse outcomes reflect the same ethnicity-based differences as those we have shown in adults (8,9). Young people with diabetes face a more prolonged exposure to the metabolic consequences of this disease than do adults. With the increasing prevalence of youth-onset type 2 diabetes, it is therefore important to understand the later impact of this emerging childhood chronic disease on affected individuals, their families and the healthcare system.

## Methods

### Study populations

This retrospective population-based cohort study examined the cumulative risks of end stage renal disease and death without end stage renal disease among Saskatchewan youth diagnosed with diabetes between January 1, 1980, and December 31, 2005. For the purposes of this investigation, youth included all children and adolescents under age 20. The study was approved by the University of Saskatchewan Research Ethics Board, and the composition of both its youth and adult populations have been described previously (7,10). Briefly, beneficiaries of Saskatchewan's universal healthcare system aged 0 to 19 years were subdivided into First Nations and non-First Nations youth using healthcare system administrative data generated by the Ministry of Health. First Nations people are indigenous to Canada and for this study

included self-identified individuals registered under Section 6 of the Indian Act of Canada and who have been assigned a 10-digit number in the Indian Registry (11). Most non-First Nations people are of European origin but about 5% are Métis, while <0.5% are nonregistered First Nations people (12). In a province of approximately 1 million people between 1980 and 2005, the First Nations population grew from about 5% to 10% of the total provincial population, and the proportion of First Nations children grew from about 7% to 18% (13) of those under 20 years of age.

Cases of diabetes were identified using an algorithm (14) recently validated in youth (15,16). This case definition requires 1 hospital discharge, 2 physician service claims or a physician service claim followed by a hospital discharge for diabetes within any 730-day period. The diabetes incident year was the first calendar year in which the case definition was met. We excluded cases occurring in adults aged 20 and older as well as female adolescents with gestational diabetes (10). End stage renal disease was identified using an algorithm that has also been described previously and that is based on fee-for-service codes for chronic dialysis and renal transplantation (8). Briefly, the end stage renal disease case definition for chronic dialysis required at least 90 days of dialysis with no break in dialysis treatment of 21 days or more. The end stage renal disease incident year was the calendar year in which chronic dialysis was initiated or a pre-emptive transplant occurred (8). For each year after the incident year for both diabetes and end stage renal disease, affected individuals were considered to represent prevalent cases. Annual prevalent counts did not include incident cases and we excluded end stage renal disease incident cases occurring before the onset of diabetes. Finally, we obtained sex, birth year, death year and loss of healthcare coverage for all study subjects.

We were not able to distinguish between type 1 and type 2 diabetes and could not identify the underlying causes of end stage renal disease. For the purposes of this study, however, end stage renal disease occurring in the same year of (or after) meeting the diabetes case definition was considered to be "diabetes-associated end stage renal disease." It should be noted, however, that when the interval between diabetes and end stage renal disease diagnoses was less than 5 years, it is more likely that some form of nondiabetic renal disease was present.

### Statistical analysis

The distributions of individual-level variables were compared between ethnic groups using *t* tests,  $\chi^2$  tests and the Fisher exact test (for small cell sizes). The significance level for all descriptive, univariate and multivariate analysis (including potential interactions) was 0.05.

We used the Fine and Gray models (17,18) to conduct a competing risks survival analysis that compared the simultaneous risks for end stage renal disease or death without end stage renal

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