



# Change in the Relation Between Age and Cardiovascular Events Among Men and Women With Diabetes Compared With Those Without Diabetes in 1994–1999 and 2014–2019: A Population-Based Cohort Study

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The risk of cardiovascular events increases exponentially with age (1). Booth et al. (1) found that in the 1990s, people with diabetes transitioned from a moderate to a high risk of cardiovascular events ~15 years earlier in life than people without diabetes. This accelerated rate of cardiovascular aging has prompted standards of diabetes care to incorporate multiple approaches to lowering cardiovascular risk, including glycemic control and the use of various cardiovascular-protective drugs. With these advances, it is unclear whether having diabetes is still equivalent to aging 15 years. We conducted a retrospective, population-based study to compare the relation between age and cardiovascular events among men and women with and without diabetes in 1994–1999 and 2014–2019.

We used administrative health care data from Ontario, Canada's most populous province. The Ontario Health Insurance Plan provides publicly funded physician- and hospital-based services for all permanent residents. We created two population-based cohorts of adults aged 20–84 years who were living in Ontario on 1 April 1994 and 1 April 2014 (index dates),

respectively. We excluded those who were ineligible for the Ontario Health Insurance Plan for 5 years before each index date. The primary exposure was diabetes status at index (any type of nongestational diabetes), based on a highly specific administrative data algorithm (2). Within each cohort, those who developed diabetes during follow-up remained in their original exposure category. Individuals were followed up for the primary composite outcome of hospitalization for acute myocardial infarction or stroke or for all-cause mortality. Individuals were followed for a maximum of 5 years after the index date and censored at departure from Ontario. Records were linked at ICES using unique, encoded identifiers.

The data set from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (e.g., health care organizations and government) prohibit ICES from making the data set publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at <https://www.ices.on.ca/DAS> (email: [das@ices.on.ca](mailto:das@ices.on.ca)).

We replicated the method originally used by Booth et al. (1) by plotting crude

outcome rates versus age-group separately for men and women in the 1994 and 2014 cohorts (four plots). We then plotted lines of best fit using exponential equations ( $y = ae^{bx}$ , where  $y$  is the outcome rate and  $x$  is age). We used these equations to solve for the age at transition from having a moderate risk of experiencing a cardiovascular event (10–19 events per 1,000 person-years) to a high risk of such an event ( $\geq 20$  events per 1,000 person-years), as described by Booth et al. (1). We also computed age-standardized sex-specific cardiovascular event rates, using the 2021 Canadian census population as the reference population, and determined the percent change in these rates across time periods. We conducted the analyses in an independent manner for each cohort, so individuals could appear in both cohorts if they fulfilled the inclusion criteria. Due to computational limitations arising from the large volume of records, we selected a random sample of 25% of each cohort. We used SAS Enterprise Guide 7.1.

The 1994 and 2014 cohorts included 1,870,791 (51.3% female) and 2,512,790 (50.9% female) people, respectively. Figure 1 shows cardiovascular event rates

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among men and women according to age-group, stratified by diabetes status. From 1994 to 2014, age-standardized cardiovascular event rates decreased by 48.3% (from 42.5 to 22.0 events per 1,000 patient-years) and 48.0% (from 30.8 to 16.0 events per 1,000 patient-years) among men and women with diabetes and by 38.8% (from 20.4 to 12.5 events per 1,000 patient-years) and 34.9% (12.4 to 8.1 events per 1,000 patient-years) among men and women without diabetes. In 1994, men and women with diabetes transitioned from having a moderate (10–19%) to high ( $\geq 20\%$ ) risk of cardiovascular events by the average ages of 45.4 and 52.3 years, respectively. These

ages were 15.6 and 15.2 years earlier than those for people without diabetes. By 2014, men and women with diabetes lived over a decade longer before transitioning to high cardiovascular risk at average ages of 56.7 and 62.8 years, respectively—only 10.1 and 10.0 years earlier than people without diabetes.

While diabetes previously conferred a degree of cardiovascular risk equivalent to aging 15 years, this gap has now been substantially narrowed to 10 years. The observed gain in years of life free from cardiovascular disease likely reflects the success of earlier diabetes screening and multifactorial management approaches that have become the modern standard of care

for diabetes. Due to limitations in our data sources, we were unable to evaluate the extent to which changes in cardiovascular risk factors, medication use, diagnostic criteria, diabetes duration, and diabetes type accounted for these patterns. However, our findings were likely driven by type 2 diabetes, which represents  $>95\%$  of our study population (3). Despite the favorable trends we observed, renewed efforts are required to reduce the persistent gap in cardiovascular events and mortality between people with and without diabetes (4), especially among high-risk subpopulations (5).

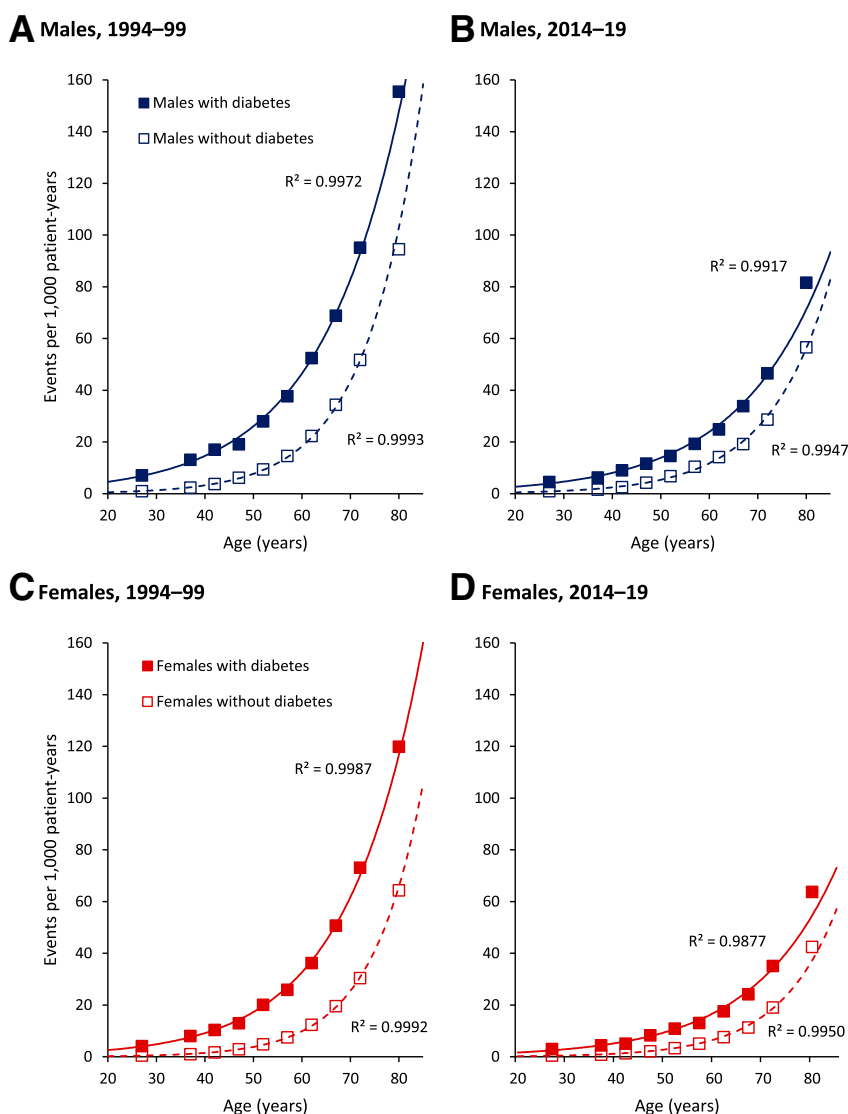
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**Author Contributions.** C.K. searched the literature, designed the study, drafted the study protocol, interpreted the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. L.L.L. acquired funding, and contributed to the study design, interpreting the data, and critically revising the manuscript for important intellectual content. L.Z. analyzed the data, and contributed to the study design, interpreting the data, and critically revising the manuscript for important intellectual content. P.C.A. contributed to the study design, interpreting the data, and critically revising the manuscript for important intellectual content. B.R.S. conceived the study, and contributed to the study design, interpreting the data, and critically revising the manuscript for important intellectual content. G.L.B. conceived the study, and contributed to the study design, interpreting the data, and critically revising the manuscript for important intellectual content. A.W. contributed to the study design, interpreting the data, and critically revising the manuscript for important intellectual content. C.K. and G.L.B. are the guarantors of this work and, as such, had full access to all the



**Figure 1**—Relation between age and rates of acute myocardial infarction, stroke, or mortality (events per 1,000 patient-years) by diabetes status and sex in 1994–1999 (A and C) and 2014–2019 (B and D). According to the method described by Booth et al. (1), each point represents an age-group (centered at each midpoint: 20–34, 35–39, 40–44, . . . , 70–74, and 75–84 years). Curves are fitted using exponential equations.

data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

### References

1. Booth GL, Kapral MK, Fung K, Tu JV. Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. *Lancet* 2006;368:29–36
2. Lipscombe LL, Hwee J, Webster L, Shah BR, Booth GL, Tu K. Identifying diabetes cases from administrative data: a population-based validation study. *BMC Health Serv Res* 2018;18:316
3. Weisman A, Tu K, Young J, et al. Validation of a type 1 diabetes algorithm using electronic medical records and administrative health care data to study the population incidence and prevalence of type 1 diabetes in Ontario, Canada. *BMJ Open Diabetes Res Care* 2020;8:e001224
4. Rawshani A, Rawshani A, Franzén S, et al. Mortality and cardiovascular disease in type 1 and type 2 diabetes. *N Engl J Med* 2017;376:1407–1418
5. Shah BR, Austin PC, Ke C, Lipscombe LL, Weisman A, Booth GL. Growing income-related disparities in cardiovascular hospitalizations among people with diabetes, 1995–2019: a population-based study. *Diabetes Care* 2023;46:751–756