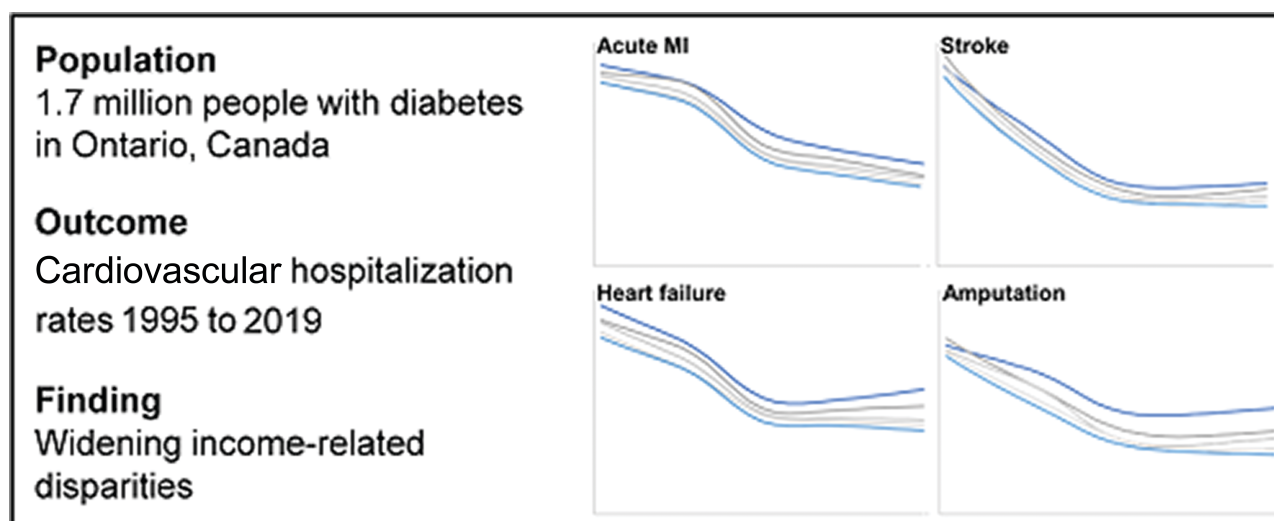


Growing Income-Related Disparities in Cardiovascular Hospitalizations Among People With Diabetes, 1995–2019: A Population-Based Study

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Diabetes Care 2023;46(4):751–756 | <https://doi.org/10.2337/dc22-1936>



ARTICLE HIGHLIGHTS

- Hospitalization rates for acute myocardial infarction (MI) among people with diabetes fell between 1995 and 2019.
- Hospitalizations for stroke, heart failure, and amputation also fell, but rates stabilized through the 2010s.
- However, there was a growing income-related disparity in this decade: rates for higher-income individuals continued to decline, whereas rates for lower-income individuals rose.



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OBJECTIVE

Cardiovascular risk reduction is an important focus in the management of people with diabetes. Although event rates have been declining over the long term, they have been observed to plateau or reverse in recent years. Furthermore, the impact of income-related disparities in cardiovascular events is unknown. The objective of this study is to evaluate age-, sex-, and income-related trends in cardiovascular hospitalization rates among people with diagnosed diabetes.

RESEARCH DESIGN AND METHODS

We calculated rates of hospitalization for acute myocardial infarction, stroke, heart failure, and lower-extremity amputation in annual cohorts of the entire population of Ontario, Canada, with diagnosed diabetes, from 1995 to 2019. Event rates were stratified by age, sex, and income level.

RESULTS

We studied nearly 1.7 million people with diabetes. The rate of acute myocardial infarction declined throughout the 25-year study period ($P < 0.0001$), such that the rate in 2019 was less than half the rate in 1995. Rates of stroke ($P < 0.0001$), heart failure ($P < 0.0001$), and amputation ($P < 0.0001$) also changed over time, but hospitalization rates stabilized through the 2010s. This apparent stabilization concealed a growing income-related disparity: wealthier patients showed continued declines in rates of these outcomes during the decade, whereas rates for lower-income patients increased (P for interaction < 0.0001 for all four outcomes).

CONCLUSIONS

During a quarter-century of follow-up, cardiovascular hospitalization rates among people with diabetes fell. However, the apparent stabilization in rates of stroke, heart failure, and amputation in recent years masks the fact that rates have risen for lower-income individuals.

Diabetes is a serious global public health problem, affecting half a billion people worldwide, or more than 10% of the adult population (1). The prevalence of diabetes continues to rise worldwide (1–3). Diabetes is an important risk factor for cardiovascular disease (CVD), and people with diabetes are at markedly increased risk for coronary

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Received 3 October 2022 and accepted 29 December 2022

This article contains supplementary material online at <https://doi.org/10.2337/figshare.21870582>.

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artery disease, stroke, and lower-extremity amputation compared with their peers without diabetes (4). In fact, CVD is a leading cause of death for people with diabetes (5–7).

As a result, cardiovascular risk reduction has increasingly become a focus of diabetes management. Optimal diabetes care includes control of cardiovascular risk factors such as hypertension and dyslipidemia, and many glucose-lowering agents have demonstrated specific protection against CVD and heart failure (8,9). Although numerous studies have documented improvements in longevity among people with diabetes (5,6,10,11), the impact of the more recent focus on cardiovascular risk reduction on the epidemiology of macrovascular diabetes complications is less well understood. Hospitalizations for CVD among people with diabetes declined in the U.S. between 1998 and 2014, with benefits similar across age, sex, and race/ethnicity categories (12). However, subsequent analyses found a resurgence in diabetes-related complication rates in the 2010s, particularly among young and middle-aged adults (13,14). There are likely many factors driving this trend, but the authors speculated that economic decline, rising unemployment, and other socioeconomic factors perpetuated by the 2008 global financial crisis could be contributors to these changes (14). However, previously published studies have not examined trends in cardiovascular complications by socioeconomic status, so these hypotheses remain untested.

We sought to evaluate trends in cardiovascular hospitalization rates among people with diagnosed diabetes over a 25-year period in Ontario, Canada, and whether these trends differed by three key demographic determinants of health: age, sex, and income level. The province's publicly funded health care system ensures universal access to hospital and physician care without deductibles or co-payments; therefore, our administrative data enable health outcomes to be examined in whole populations over time. Canada experienced an economic downturn following the global financial crisis, with lower-income groups being disproportionately affected (15). Therefore, we hypothesized that improvements in diabetes-related cardiovascular hospitalization rates

over time were diminished after 2008, particularly in lower-income populations.

RESEARCH DESIGN AND METHODS

The study used population-level health care administrative databases in Ontario, Canada's most populous province. These databases included the Discharge Abstracts Database, which includes detailed information on all hospital admissions in Ontario; the Ontario Health Insurance Plan database, which includes information from fee-for-service billing claims submitted by all Ontario physicians; and the Registered Persons Database, which includes demographic information on all Ontario residents. These data sets were linked using unique encoded identifiers and analyzed at ICES (formerly the Institute for Clinical Evaluative Sciences). The Discharge Abstracts Database has been validated in a reabstraction study that found almost perfect agreement ($\kappa > 0.8$) for cardiovascular diagnoses (16).

We created annual cohorts from 1995 to 2019 of the entire population of Ontario with diagnosed diabetes as of 1 April each year. Diabetes was identified using a highly specific validated definition of diabetes, derived from the hospitalization and physician claims data, that has 99.1% specificity and 91.4% positive predictive value (17). We then looked forward for 1 year to identify hospitalizations with a primary diagnosis of acute myocardial infarction, stroke, heart failure, and nontraumatic lower-extremity amputation. We also examined hospitalizations for acute appendicitis as a negative control outcome, where no association with changes to diabetes care or risk factors over time was expected. Coding for each outcome is presented in Supplementary Table 1. Individuals who died or lost eligibility for health care coverage because they left the province were censored at the time of death/loss of eligibility, and thus contributed less than a full year of follow-up. Only one hospitalization per year per individual was counted for each diagnosis. For each patient and in each annual cohort, we determined age (grouped as ≤ 29 years, then by decade up to ≥ 80 years), sex, and income level. Income was determined ecologically, based on the average income per single-person equivalent for each individual's neighborhood of residence. Neighborhoods were defined by dissemination area, a small area defined by Statistics Canada

with an average population of around 500 people that is relatively homogeneous with respect to social characteristics. Neighborhoods are ranked and divided into quintiles within their metropolitan area, then pooled across areas and across time; therefore, specific income thresholds separating each group are not available. Although this measure of income level is ecologic, there is evidence to suggest that neighborhood-level income is a good proxy for socioeconomic status when individual-level income is unavailable (18).

We used Poisson regression to model the hospitalization rate as a function of year. To do so, we fit a model to the individual-level data, using generalized estimating equation methods to account for the same individual being in multiple annual cohorts. The dependent variable was whether a subject experienced a hospitalization in the given year, with the duration of follow-up during that year used as an offset. The relationship between calendar year and the logarithm of the outcome rate was modeled using restricted cubic splines with four knots. The regression coefficients from the Poisson model were used to plot the modeled rate and 95% CI of each outcome between 1995 and 2019, and we tested whether the hospitalization rate changed over time (i.e., did the trend in hospitalization rate over time differ from the horizontal). We then fit three models for each outcome, in each case adding one baseline factor (age, sex, and income) and an interaction term between the baseline factor and year. The modeled rates were plotted to demonstrate age-, sex-, and income-stratified hospitalization rates over time for each outcome. The statistical significance of the interaction term was used to test whether the trend in the hospitalization rates over time differed between strata. To examine changes in income-related gradients over time, we divided the highest modeled income-stratified rate by the lowest for each outcome in each year. Models were fit using the GENMOD procedure in SAS/STAT release 14.3.

The use of the data in this project is authorized under section 45 of Ontario's Personal Health Information Protection Act, and therefore does not require review by a Research Ethics Board.

The data from this study are 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>.

RESULTS

We evaluated 1,697,504 people with diabetes, who were followed for a median of 9.2 years (interquartile range 4.5–15.0), and a total of more than 17.5 million person-years of follow-up. The baseline characteristics of the 1995, 2003, 2011, and 2019 cohorts are presented in Supplementary Table 2. The rate of acute myocardial infarction among people with diabetes declined (Fig. 1A, $P < 0.0001$), such that the rate in 2019 (7.2 hospitalizations per 1,000 person-years) was less than half the rate in 1995 (15.4 per 1,000 person-years). Comparable declines between 1995 and 2019 were seen in the rates of stroke (10.8 to 3.9 hospitalizations per 1,000 person-years), heart failure (29.8 to 15.9 hospitalizations per

1,000 person-years), and amputation (4.4 to 2.1 hospitalizations per 1,000 person-years) (Fig. 1B–D, respectively; $P < 0.0001$ for each outcome). However, most of the decline for these last three outcomes occurred between 1995 and the late 2000s; their rates in 2010 (3.7, 15.3, and 2.1 hospitalizations per 1,000 person-years, respectively) were, in fact, similar to those in 2019.

Stratification by income (Fig. 2 and Supplementary Table 3) showed that the plateau in overall rates of stroke, heart failure, and amputation in the 2010s concealed a growing income-related disparity: higher-income patients showed decreasing rates of all of these outcomes during this decade, whereas hospitalization rates among lower-income patients were increasing (P for interaction < 0.0001 for all four outcomes). For example, hospitalization rates for heart failure decreased from 13.8 per 1,000 person-years in 2010 to 13.1 per 1,000 person-years in 2019 for the highest-income patients, whereas they rose from 17.3 to 19.4 per 1,000 person-years in the

same time period for the lowest-income patients. Fig. 3 shows the income-related gradient for each outcome over the study period. In 1995, income-related gradients were modest, between 1.10 and 1.18 for all four CVD outcomes. Income-related gradients grew for all outcomes over time, such that, by 2019, the ratio of the hospitalization rate in the lowest-income group compared with the highest-income group was 1.29 for acute myocardial infarction, 1.37 for stroke, 1.49 for heart failure, and 1.78 for amputation.

Stratification by sex is presented in Supplementary Fig. 1 and Supplementary Table 4. Males with diabetes were at higher risk than females for myocardial infarction and especially for amputation, and the relative difference between sexes grew over time (P for interaction < 0.0001 for both). Absolute hospitalization rates for stroke and heart failure were similar between sexes, although the difference in trends over time was statistically significant because of the study's large sample size (P for interaction = 0.005 for stroke, < 0.0001

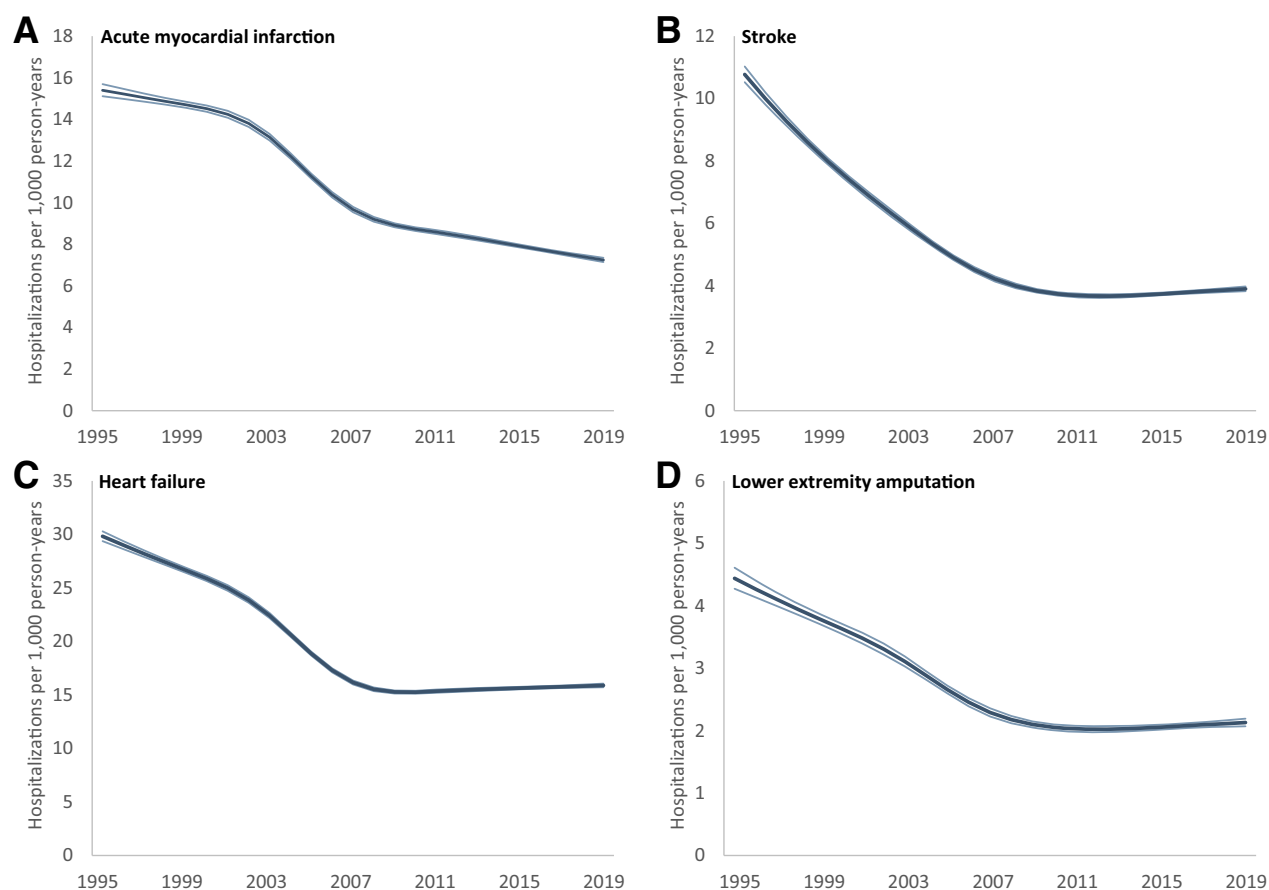


Figure 1—Rates (with 95% CI) of hospitalization for acute myocardial infarction (A), stroke (B), heart failure (C), and lower-extremity amputation (D) among people with diagnosed diabetes, 1995–2019.

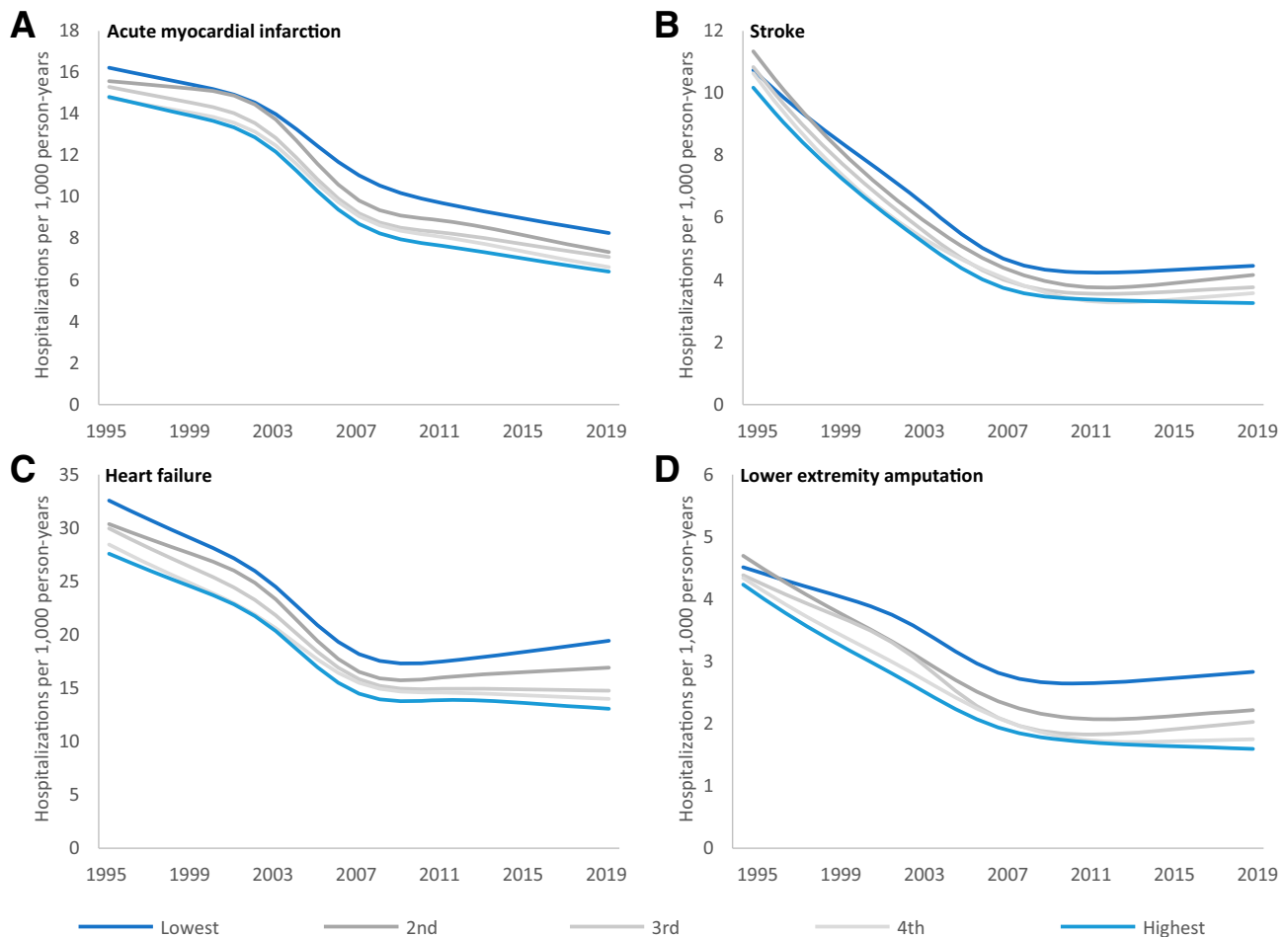


Figure 2—Rates of hospitalization for acute myocardial infarction (A), stroke (B), heart failure (C), and lower-extremity amputation (D) among people with diagnosed diabetes, 1995–2019, stratified by income.

for heart failure). Stratification by age (Supplementary Fig. 2 and Supplementary Table 5) showed the expected age-related gradient in CVD risk, with relatively greater declines in myocardial infarction and stroke risk in older age groups (P for interaction < 0.0001 for all four outcomes).

We also examined rates of hospitalization for acute appendicitis as a negative control outcome, where no association with changes in diabetes care or risk factors over time was expected. Rates rose over time (Supplementary Fig. 3A, $P < 0.0001$). The trend in hospitalization rates over time did not differ by age (Supplementary Fig. 3B, $P = 0.07$) or by income (Supplementary Fig. 3D, $P = 0.5$), but the trend between sexes was not parallel (Supplementary Fig. 3C, $P = 0.01$).

CONCLUSIONS

During a quarter-century of follow-up, cardiovascular hospitalization rates among people with diabetes fell. This improvement

may be attributed to more intensive control of cardiovascular risk factors, and improved identification and management of people with high cardiovascular risk. Rates of acute myocardial infarction continued to decline even into the last years of the observation period, whereas the rates of stroke, heart failure, and amputation mostly stabilized in the last decade. However, this apparent stabilization masks the fact that rates of these three complications, in fact, rose for lower-income individuals during this time. Similarly, the relative risk for men versus women grew significantly for acute myocardial infarction and amputation but not to a clinically important magnitude for stroke or heart failure. Several possible changes in clinical care could have contributed to the overall decline in cardiovascular hospitalization rates, including a greater focus on cardiovascular risk reduction as a key component of diabetes care, the adoption of lower targets for blood pressure and cholesterol management, and the introduction of newer

glucose-lowering agents that have favorable effects on CVD. The fact that disparities grew for men versus women and for lower-income people versus higher-income people suggests that these cardiovascular risk-reducing strategies were being applied or adopted equitably.

The overall findings of this study parallel those seen elsewhere. Hospitalization for acute coronary syndromes, ischemic stroke, and heart failure declined between 1998 and 2014 for people with diabetes in a nationally representative sample in the U.S., with declines seen across age groups, sexes, and race/ethnicity categories (12). Earlier studies also showed declines in cardiovascular hospitalizations between the 1990s and early 2010s (19–22). Similarly, mortality due to CVD, ischemic heart disease, and stroke declined between 1988 and 2015 in a representative sample of Americans with diabetes (23). While these studies all showed declining rates of complications over time, other American studies echoed our findings of stabilizing or

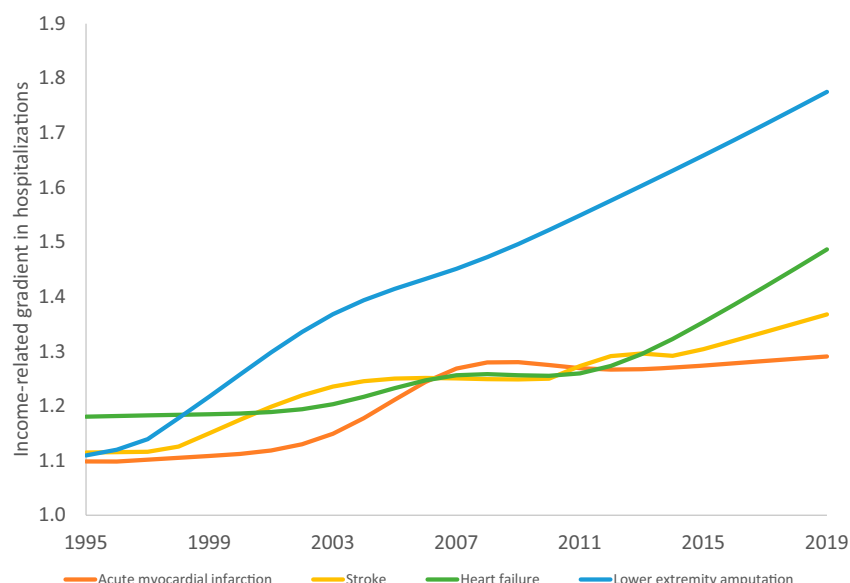


Figure 3—Income-related gradients for cardiovascular hospitalizations among people with diagnosed diabetes, 1995–2019.

even increasing rates of cardiovascular complications in more recent years (14). For example, the increase in amputations between 2010 and 2015 reversed nearly one-third of the previous 20-year decline (13). Diabetes complication rates rebounded in young and middle-aged adults, whereas long-term declines plateaued among older adults. Reasons for this turnaround were not clear, but the authors speculated that changes in health policy (such as high-deductible health plans) or changes in access to care could be causes (13). However, these speculative explanations are less likely to contribute to worsening complication rates in Canada. The health care system ensures access for all residents to hospital and physician care, without co-payments or deductibles impacting access. In addition, the dramatic increase in the price of insulin in the U.S. was not emulated north of the border (24,25). The price of a vial of insulin in the U.S. increased from USD 40 in 2001 to USD 275 in 2019 (26), whereas the price of a vial of insulin lispro in Canada rose from CAD 23 in 2001 to CAD 31 today. Another possibility is that the 2008 global financial crisis contributed to these unfavorable trends as a significant socioeconomic determinant of health. Although the crisis had a lower impact in Canada than in the U.S., it disproportionately affected lower-income Canadians (15). We found rising income-related disparities in cardiovascular hospitalizations, especially for amputation, thus supporting the

hypothesis that socioeconomic factors contribute to the resurgence of diabetes-related complications. Lower-income patients continue to face disparities in care and barriers to accessing health resources, even with a universal publicly funded health care system (27). They may also face a higher prevalence of risk factors like smoking and obesity, greater food insecurity, and more mental health problems. Importantly, we did not observe a similar widening in income-related disparities for an unrelated outcome, acute appendicitis, which strengthens the inference, from this observational study, that income-related disparities in diabetes outcomes are growing.

The reasons for this increasing income-related disparity warrant further investigation. For example, socioeconomic disparities in cardiovascular risk factors have widened in Canada (28). In addition, unlike hospital and physician care, medications are not a universally insured benefit for Ontario residents, and nearly three-quarters of the population relies on private insurance or is uninsured (29). Hence, the increasing use of newer, more expensive glucose-lowering agents that also reduce cardiovascular risk could be a factor in growing income-related disparities in cardiovascular outcomes toward the end of the study period. There is a large body of evidence supporting associations of socioeconomic status, neighborhood environment, and other social determinants of health with diabetes-related outcomes in the U.S. (30), and we have previously

demonstrated income-related disparities in our province (31–34). These disparities will grow as optimal diabetes management continues to require more and costlier medications. Furthermore, the enduring economic fallout of the COVID-19 pandemic has impacted employment, health insurance coverage, and income inequality worldwide, and hence continued growth in income-related inequities may well result in mounting numbers of avoidable cardiovascular hospitalizations for lower-income people with diabetes.

Our study has a number of strengths. The single-payer universal health care system in Canada means that our data include all CVD hospitalizations among all people diagnosed with diabetes, with no loss to follow-up or missing data. In addition, this study represents the entire population of Canada's most populous province and is not limited to a sample or to a single region or insurer. Third, the absence of user fees or deductibles to access physician and hospital care ensures that these factors do not contribute to the observed findings, though, as noted earlier, lower-income patients in Canada continue to face other economic barriers to optimal care. Fourth, our longitudinal data ensure that we are able to use a single data source and methodology to follow the population for a quarter-century. Finally, we also study acute appendicitis as a negative control outcome to detect biases that would lead to spurious noncausal inferences. The absence of age- or income-related differences in the trends in appendicitis hospitalizations provides support for the study's conclusions. However, there are some limitations to the analysis to highlight. Changes in clinical care and hospitalization pathways over the 25 years of the study could have contributed to changes in CVD hospitalization rates independently of disease burden. In the cohort, we cannot separate diabetes types; however, the overwhelming majority of the population with diabetes has type 2 (35). It is possible that greater screening for diabetes led to its diagnosis earlier in the natural history of disease and, hence, a lower risk of complications in the population diagnosed with diabetes (36). However, based on a recent analysis, screening rates in Ontario remained fairly stable during the period in which the greatest decline in complication rates was observed (37). Income cannot be ascertained at an individual level but is assigned

ecologically using a good proxy (18). Finally, we are only able to describe the changes in cardiovascular hospitalization rates over time; we are unable to attribute causality to any specific clinical or policy intervention.

In conclusion, the cardiovascular hospitalization rates among people with diabetes have fallen over the past 25 years. While acute myocardial infarction rates continue to fall, the declines in the rates of stroke, heart failure, and amputation have stabilized over the past decade. However, this apparent stabilization masks a growing income-related disparity in cardiovascular outcomes among people with diabetes.

Funding and Duality of Interest. This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and the Ministry of Long-Term Care. Parts of this material are based on data and information compiled and provided by the Canadian Institute of Health Information. B.R.S. receives support from the University of Toronto as the Novo Nordisk Research Chair in Equitable Care of Diabetes and Related Conditions. P.C.A. is supported by a Mid-Career Investigator Award from the Heart and Stroke Foundation. C.K. reports consulting fees and honoraria from Sanofi, Abbott, and AstraZeneca. L.L.L. receives support as the Director of the Novo Nordisk Network for Health Populations at the University of Toronto. No other potential conflicts of interest relevant to this article were reported.

The analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

Author Contributions. All authors were involved in the conception and design of the study and the interpretation of the results. B.R.S. wrote the first draft, and all authors edited, reviewed, and approved the final version. B.R.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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