The Incidence of Diabetic Ketoacidosis During "Emerging Adulthood" in the USA and Canada: a Population-Based Study

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BACKGROUND: As children with diabetes transition to adulthood, they may be especially vulnerable to diabetic ketoacidosis (DKA). Cross-national comparisons may inform efforts to avoid this complication.

OBJECTIVE: To compare DKA hospitalization rates in the USA and Manitoba, Canada, during the vulnerable years known as "emerging adulthood."

DESIGN: Cross-sectional study using inpatient administrative databases in the USA (years 1998–2014) and Manitoba, Canada (years 2003–2013).

PARTICIPANTS: Individuals aged 12–30 years hospitalized with DKA, identified using ICD-9 (USA) or ICD-10 codes (Manitoba).

MAIN MEASURES: DKA hospitalization rates per 10,000 population by age (with a focus on those aged 15–17 vs. 19–21). Admissions were characterized by gender, socioeconomic status, year of hospitalization, and mortality during hospitalization.

KEY RESULTS: The DKA rate was slightly higher in the USA among those aged 15–17: 4.8 hospitalizations/10,000 population vs. 3.7/10,000 in Manitoba. Among those aged 19–21, the DKA hospitalization rate rose 90% in the USA to 9.2/10,000, vs. 23% in Manitoba, to 4.5/10,000. In both the USA and Manitoba, rates were higher among those from poorer areas, and among adolescent girls compared with adolescent boys. DKA admissions rose gradually during the period under study in the USA, but not in Manitoba.

CONCLUSIONS: In years of "emerging adulthood," the Canadian healthcare system appears to perform better than that of the USA in preventing hospitalizations for DKA. Although many factors likely contribute to this difference, universal and seamless coverage over the lifespan in Canada may contribute.

KEY WORDS: healthcare access; diabetic ketoacidosis, emerging adulthood.

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INTRODUCTION

The years that follow adolescence—a period developmental psychologists describe as "emerging adulthood"—are a time of exploration, but also vulnerability, particularly for those with illnesses like diabetes mellitus.[1–4] During this period, many young people leave home, gain independence, transition from pediatric to adult medical care (often rupturing the continuity of their healthcare), and, in the USA, lose health insurance.[2, 4, 5] For some in this age group, disordered eating and substance use increase, while new health problems accrue.[1, 2] These changes put these individuals at increased risk for non-adherence to insulin and thus acute complications, like diabetic ketoacidosis (DKA).

DKA is dangerous and costly,[6–8] but it is fortunately also largely preventable.[6] As one of many "ambulatory care sensitive conditions"—complications that good ambulatory care can prevent—DKA rates are a proxy measure of outpatient quality and access to care.[9, 10]

Using large inpatient databases, we investigated DKA hospitalizations among adolescents and emerging adults in the USA and in Manitoba, Canada. We focused on these age groups because it is a time of particularly sharp differences between the two nations in insurance coverage and continuity of primary care. In Canada, a single-payer system assures universal, seamless coverage across the lifespan, while family physicians provide most primary care. In contrast, emerging adults in the USA usually change insurance coverage and physicians, and many become uninsured. We hypothesized that these health financing and organizational factors might confer an advantage to Canada in the prevention of DKA.

METHODS

Data Sources

For the USA, we analyzed data from the National Inpatient Sample (NIS) (previously known as the Nationwide Inpatient Sample) for 1998–2014. Prior to 2012, the NIS consisted of all hospitalizations from a 20% sample of US hospitals; since then, it has consisted of a 20% sample of hospitalizations from all US hospitals. Because Texas and Pennsylvania grouped age in 5-year categories for at least some children, we excluded those states for years prior to 2012, when the NIS stopped including state identifiers.

The NIS data includes up to 25 diagnoses for each admission, coded using the ICD-9. We identified all hospitalizations among persons aged 12–30 whose primary diagnosis was DKA or a closely related condition, such as diabetes with hyper-osmolarity or diabetes with other coma (online appendix); these hospitalizations are henceforth referred to as "DKA hospitalizations." We repeated our main analysis using only the four most specific ICD-9 DKA codes (250.10, 250.11, 250.12, and 25.13), which accounted for 97% of the hospitalizations identified using our broader definition, and found virtually identical results, which we do not report further.

To estimate population denominators for calculation of DKA rates, we analyzed the Census Bureau's Current Population Survey (CPS) Annual Social and Economic Supplements for 1999–2015, which provide data for the preceding calendar year. For years prior to 2012, we excluded individuals from Texas and Pennsylvania.

We obtained data on hospitalizations in the province of Manitoba for the years 2004–2013 from the Population Research Data Repository at the Manitoba Centre for Health Policy at the University of Manitoba. The Manitoba data included 100% of hospitalizations, and tabulated diagnoses based on ICD-10-CA codes,[11] which we aligned with the US ICD-9 codes. Patients aged 12–30 were included if they had a code for DKA or a related condition (online appendix). We also performed the analyses using a broader set of diabetes-related codes (online appendix), which yielded somewhat higher rates, but otherwise similar results, which we do not report further. The repository contains a complete population registry file, which was used to calculate the denominator for hospitalization rates.

Analysis

Our primary outcomes were age-specific annualized DKA hospitalization rates. For this, and most other analyses, we averaged data for all study years. All analyses were carried out using SAS version 9.4 (Cary, NC) and (for the USA) employed weights provided by the NIS that produce national estimates, and SAS procedures that account for complex sampling.

Our main analyses examined age trends in DKA hospitalization rates per 10,000 population in the USA and Manitoba, and particularly cross-national differences before and after age 18, the age at which multiple transitions often occur, including movement out of the family of origin, loss of eligibility for public insurance in the USA (Medicaid), and change from pediatric to adult medical physicians. We estimated hospitalization rates in the USA and Manitoba for a "before" subgroup (ages 15–17) and an "after" subgroup (ages 19–21). For this comparison, we excluded those aged 18 years because, in the USA, major insurance transitions often occur between the 18th and 19th birthdays. We then calculated the difference in hospitalization rates in the "before" and "after" groups in the USA and Manitoba.

We characterized US patients by insurance status at discharge (dichotomized as insured or uninsured), race (although many states do not report race), sex, year of hospitalization, and in-hospital death (using the NIS "died" variable, which is based on discharge disposition records). As a proxy for socioeconomic status, we used median income of the patient's ZIP code of residence (categorized into quartiles). This ZIP code income analysis was carried out only for the years 2003–2014 because prior to 2003, the NIS defined the ZIP code income variable differently. Patients hospitalized in Manitoba were characterized by postal code income quintile (derived from Canadian census dissemination area data), sex, in-hospital death, and year of hospitalization.

To calculate DKA hospitalization rates in the USA, we used corresponding CPS estimates for the denominator (e.g., hospitalization rates of the uninsured used CPS estimates of the uninsured as the denominator). For the ZIP code income quartile analysis, the denominator was the total population estimate divided by 4. For Manitoba, we used actual population figures for each postal code income quintile.

We calculated mean charges for US DKA hospitalizations for 2014 using the NIS' variable for total charges. To estimate "excess" DKA hospitalizations in the USA for persons aged 18–30, we first calculated the expected hospitalization rate had the rise in the US hospitalization rate between ages 15–17 and ages 18–30 been equal to the change with age in Manitoba. We then subtracted this "expected" rate from the observed rate, and used this excess rate and mean charges per DKA hospitalization to estimate total excess DKA spending for those aged 18–30.

The study was deemed exempt from review by the Institutional Review Board of the Cambridge Health Alliance.

RESULTS

We identified and analyzed 168,946 patients hospitalized with DKA in the USA and 1278 in Manitoba. Table 1 presents characteristics of these patients. In the USA, 41.7% were nonwhite, 52.5% were female, and 20% were uninsured. A large share of admitted youths resided in lower income ZIP codes. Similarly, in Manitoba, 52.3% of hospitalized DKA patients were female and were also disproportionately from lower income areas.

Figure 1 (panel a) displays DKA hospitalization rates by age in the USA and Manitoba. In the USA, the rate was 4.2/

Table 1 Selected Characteristics of Patients Ages 12–30 Hospitalized with DKA in the USA and Manitoba

	USA	Manitoba
	(*n* = 168,946)	(*n* = 1278)
Race		
White	58.3%	–
Black	25.0	
Hispanic	12.3	
Asian or Pacific Islander	0.9	
Native American	0.8	
Other	2.8	
Sex		
Male	47.5	47.7%
Female	52.5	52.3
Insurance		
Uninsured	20.0	0
Insured	80.0	100*
ZIP/postal code income quartile (USA) or quintile (Manitoba), lowest to highest		
1	36.0	29.7
2	28.1	24.7
3	21.8	20.7
4	14.1	14.9
5	–	9.9

DKA diabetic ketoacidosis. In the USA, 35,795 had missing data on race, 357 on sex, 580 on insurance status, and 3199 on ZIP code income quartile. For ZIP code income, percentages reflect years 2003–2014. Race data were not available for Canada
**Data on percent population insured in Canada are for overall Canadian population and are drawn from OECD health statistics*[12]

10,000 at age 15, after which it began rising, peaking at 9.7/10,000 at age 19. In Manitoba, the DKA hospitalization rate remained below 4.0/10,000 until age 17, and peaked at 5.4/10,000 at age 24. Figure 1 (panel b) shows the corresponding uninsurance rates by age (averaged across study years) for the overall US population, which rose from 12.8% at age 17 to 23.6% at age 19 and 31.7% at age 23; in contrast, Canada has close to 100% population insurance coverage.[12]

Figure 2 displays the DKA hospitalization rates in the USA and Manitoba for the "before" (ages 15–17) and "after" (ages 19–21) subgroups. In the "before" group, the rate was 4.8/10,000 in the USA and 3.7/10,000 in Manitoba. In the USA, the rate increased to 9.2/10,000 (a 90% rise) in the "after" group, while in Manitoba, it increased only 23% to 4.5/10,000.

Figure 3 shows US DKA hospitalization rates by age and income quartile of the patients' ZIP code. DKA hospitalizations were more frequent in lower income ZIP codes, a difference that widened after age 18. Among residents of the highest income ZIP codes, the hospitalization rate increased 84.4% between the before (ages 15–17) and after (ages 19–21) subgroups, vs. an increase of 117.7% for residents of the lowest income ZIP codes.

Lower income also predicted DKA hospitalizations in Manitoba; rates were 2.0/10,000 in the highest income quintile, rising to 5.4/10,000 in the lowest. DKA hospitalization rates rose as youths entered emerging adulthood in all quintiles except the highest (online appendix, E-Figure 1).

The in-hospital DKA mortality rate increased with age in the USA, from 0.5 per million population for ages 12–17, to 0.9 per million for ages 18–23, and to 1.4 per million for ages 24–30. No inpatient DKA deaths occurred in Manitoba during the study period.

DKA hospitalization rates were higher for females than those for males in the USA from ages 12 to 25, especially in adolescence, with a peak female-to-male ratio of 1.4 at age 16. However, after age 25, the DKA hospitalization rate for men exceeded that of women. A spike in the female-to-male ratio during adolescence was also observed in Manitoba, peaking at 2.7 at ages 16 and 17 (online appendix, E-Figure 2).

In the USA, the rate of DKA hospitalizations among the uninsured (6.1/10,000) was slightly lower than that among the insured (7.0/10,000), a difference that was most marked among children but was attenuated at older ages, as DKA hospitalizations rose more steeply among the uninsured in the early years of emerging adulthood. These insurance figures should be interpreted cautiously since a hospitalization for diabetes may cause some persons, especially children, to gain public coverage through a variety of mechanisms, potentially confounding the relationship between DKA and insurance.

The DKA hospitalization rate increased over time in the USA, from 5.1/10,000 in 1998 to 8.9/10,000 in 2014. In contrast, in Manitoba, DKA hospitalizations declined from 2003 to 2013 (online appendix, E-Figure 3).

Charges for a DKA hospitalization in the USA averaged $21,445 in 2014. If the difference between US and Manitoban DKA hospitalization rates among those aged 15–17 (4.8/10,000–3.7/10,000, or 1.2/10,000) had persisted for those aged 18–30, the US DKA hospitalization rate among those aged 18–30 would have been 2.2/10,000 lower. Based on this figure, the cost of "excess" DKA hospitalizations in the USA totaled $263.1 million in 2014.

DISCUSSION

DKA hospitalization rates increased during emerging adulthood in both the USA and Manitoba, but this rise was far steeper in the USA. While DKA hospitalization rates were higher among US residents of poorer ZIP codes at all ages, this disparity widened after age 18, implicating socioeconomic factors as contributors to the US upswing. However, disparities in DKA hospitalization rates by income exist in Manitoba as well. Additionally, DKA hospitalization rates appeared to rise over time in the USA but not in Manitoba. Overall, our results suggest that the Canadian healthcare system may be better at preventing DKA during the transition to emerging adulthood.

Differences in diabetes prevalence are unlikely to explain the cross-national differences we observed. While diabetes prevalence among adults (most of whom have type II diabetes) is higher in the USA than in Canada,[13] this is not the case for young people, where type I diabetes predominates. Among people younger than 20, the prevalence of diabetes in the USA in 2009 was 0.2%,[14] while in Canada, the figure (excluding those less than 1 year old) was 0.3% around the same time.[15] In 2015, the estimated incidence of type I diabetes among children

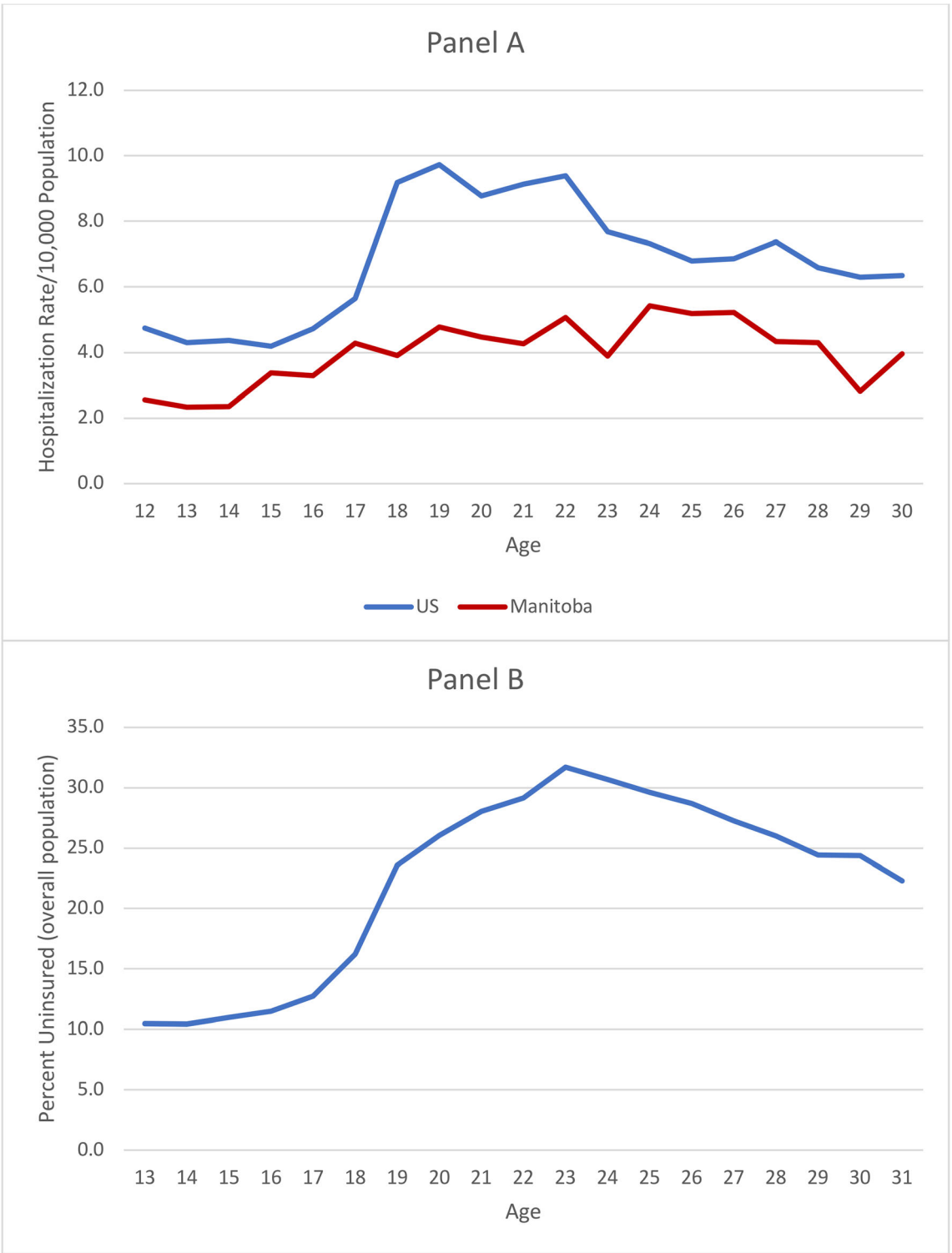

Figure 1 DKA hospitalization rates (panel a) and overall US population uninsurance (panel b) rates by age. DKA, diabetic ketoacidosis.

under age 15 was slightly higher in Canada than in the USA.[16] Additionally, in our study, DKA hospitalization rates in the nations were similar in childhood, sharply diverged in early adulthood, and then converged somewhat in the mid-20s, a pattern that cannot be explained by differences in prevalence.

One possible cause of a USA-Canada difference is that emerging adults in the USA frequently undergo health insurance disruptions, including loss of coverage, while Canada offers universal, seamless coverage. In the USA, children more readily qualify for coverage under Medicaid than adults. Prior to the implementation of the Affordable Care Act, the median state eligibility threshold was 235% of the federal poverty line for children,[17] vs. 61% for working parents.[18] Moreover, many states had simplified enrollment procedures

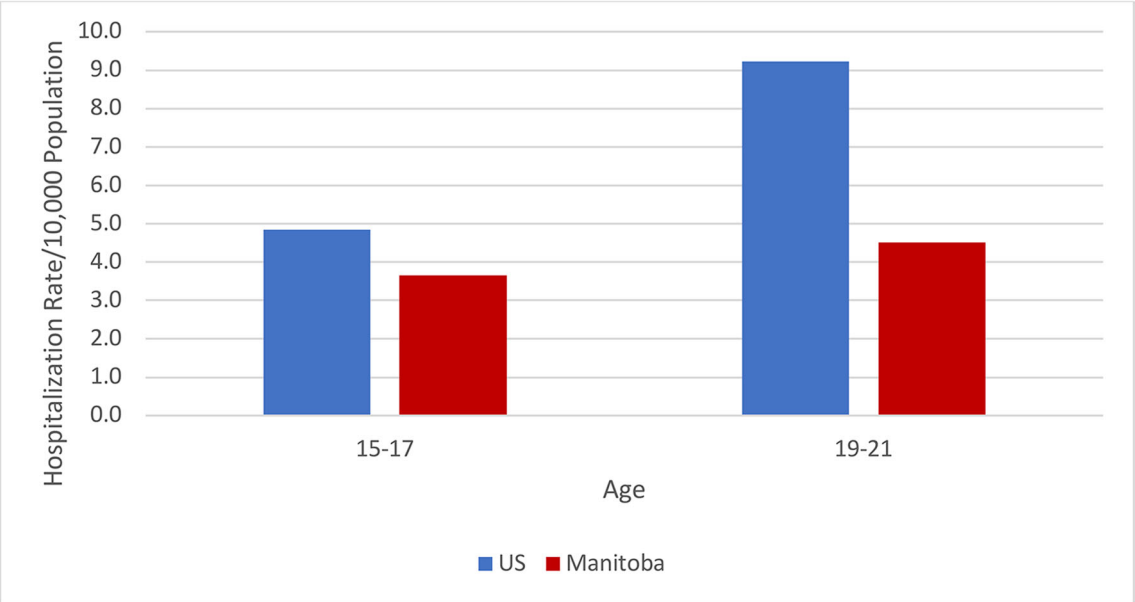

Figure 2 DKA hospitalization rates: age 15–17 and 19–21. DKA diabetic ketoacidosis.

or special programs for children that made it easier for them to obtain public coverage.

However, while the ACA lifted the Medicaid eligibility threshold for adults to 138% of the FPL in states that accepted the Medicaid expansion, eligibility standards for adults remain much more stringent than for children. Consequently, as of 2016, public programs covered 41.5% of children younger than 19, vs. 23.1% of those aged 19 to 25.[19] And notably, undocumented immigrants, including children, continue to face additional barriers in the USA: they cannot purchase subsidized insurance on the ACA's marketplaces or, for the most part, participate in Medicaid.

However, even those emerging adults who remain covered over time frequently face disruptive insurance transitions in the USA. Until 2010, most private family plans terminated a dependent child's coverage at age 18 or 19, although the ACA raised this threshold to 26. Changes in coverage often require changing doctors since many insurance plans have narrow provider networks; such "churn" has known harmful effects.[20]

Our observation that relatively few young people hospitalized with DKA in the USA were uninsured likely reflects reverse causation. Insurance status in the NIS is defined at the time of discharge, and hospital social workers often arrange coverage for uninsured patients (especially retroactive

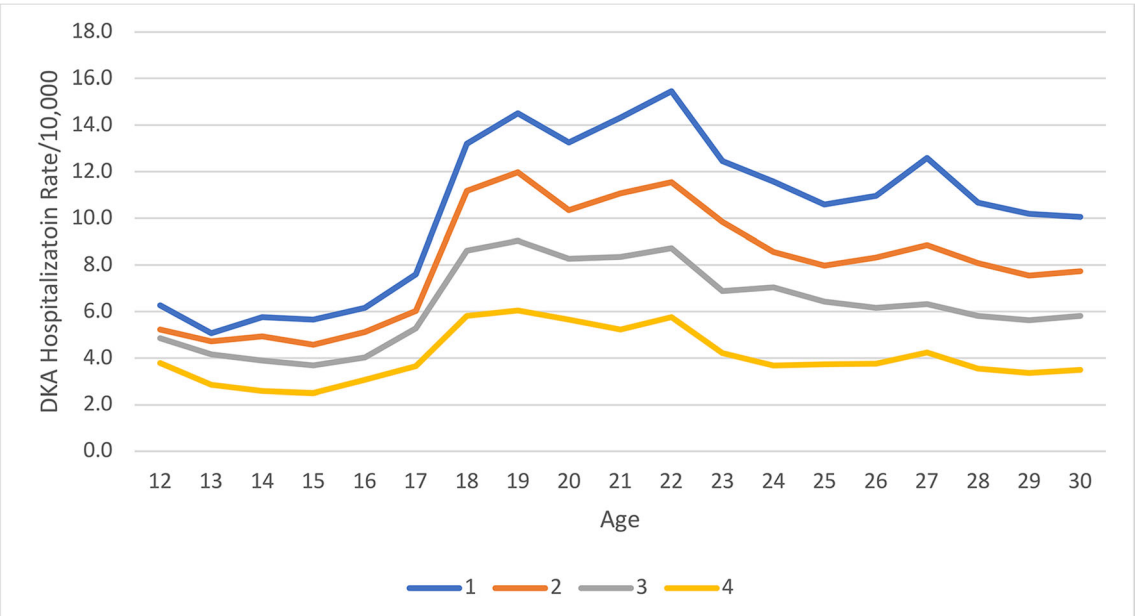

Figure 3 US DKA hospitalization rate/10,000 by ZIP code income quartile. 3199 hospitalization records had missing data on ZIP code income quartile. DKA, diabetic ketoacidosis. Quartile 1, lowest; quartile 4, highest.

Medicaid coverage) during a hospital stay. Hence, insurance coverage of DKA patients at hospital discharge may not reflect their coverage prior to hospital admission. Not surprisingly (given the age-based eligibility differences), uninsured DKA hospitalizations increased sharply after age 18.

However, multiple factors could have contributed to our results. For instance, underinsurance in the USA may have played a role. While Medicaid generally requires no, or very low, copayments or deductibles, most Americans with private insurance face significant cost-sharing for physician services, hospitalizations, and medications. Prescription drug cost-sharing reduces adherence to insulin[21] and discontinuation of insulin because of cost can lead to DKA.[22] Underinsurance also reduces the use of diabetic specialty care: patients with diabetes transitioned into high-deductible healthcare plans are less likely to see a specialist, and, among those with low incomes, more likely to visit the ER for diabetes-related complications.[23] In Manitoba, patients pay nothing for physician or hospital services, but must pay an annual, income-related deductible before medications become fully covered, although those on social assistance do not pay any deductible.

While coverage-related barriers to care increase acute complications from conditions like diabetes,[24–28] and likely explain some of the US/Canada differences we observed, other factors probably also play a role. Cultural differences between pediatric and adult specialty care, declining parental oversight, increased financial independence and strain, and a difficult-to-navigate adult healthcare landscape could all contribute to poor outcomes for emerging adults with diabetes.[1, 2] About one-third of individuals aged 22–30 at one US diabetes center, for instance, experienced a 6-month gap between pediatric and adult endocrinology visits.[29]

Several organizational factors in Manitoba might mitigate care disruptions. Most primary care in Canada is delivered by family doctors, minimizing age-related primary care transitions. Although the vast majority of children with type I diabetes in Manitoba (including 95% of those under age 14) are cared for by the specialized diabetes program at the Children's Hospital in Winnipeg,[30] the continuity provided by family practitioners may provide a useful backstop during the transition from pediatric to adult specialty care. Starting in 1995, the Winnipeg center also implemented a program designed to transition adolescents aged 13–18 into adult medical care.[31] A second program, launched in 2002 to provide navigators and other resources to guide diabetic teens into the adult medical care system,[31, 32] apparently reduced the proportion of emerging adults who dropped out of medical care, although not DKA rates.[32]

Finally, non-medical factors, such as youth mobility, may come into play. US emerging adults may be slightly less likely to reside in their parental home.[33, 34]

While overall age trends and cross-national differences were our main focus, other patterns are also notable. The spike in hospitalization rates we observed in both nations among adolescent females as compared with males does not reflect the epidemiology of type I diabetes, which affects males and females at similar rates.[35] This disparity may instead reflect young females' higher rates of disordered eating, or insulin omission for the purpose of weight loss—both of which are risk factors for DKA.[2]

Our finding of a socioeconomic gradient in DKA hospitalizations in both nations is consistent with previous findings connecting socioeconomic status (and area-level deprivation) with DKA.[36] The higher incidence of DKA among lower income youths likely reflects a combination of factors, including poorer healthcare access in the USA, as well disparities in health literacy and food security in both nations.

Some limitations of our study should be noted. The data we analyzed represent hospitalizations, not individuals. Hence, we cannot differentiate first episodes of DKA from recurrent admissions. Additionally, we used income in patients' postal code as a proxy for socioeconomic status, an imperfect measure. Manitoba's experience may not be entirely typical of Canada-wide trends. The time period of study differed between the populations, but substantially overlapped. The two nations used different versions of the ICD coding system, although coding artifacts could not explain differing age trends. Finally, our study design does not allow us to definitively prove that differences in insurance coverage caused the differences we observed.

A century ago, young people with diabetes could expect to live for a year or two following diagnosis.[37] The development of insulin at the University of Toronto in 1922 was a milestone, transforming DKA from a death sentence to a treatable illness. Today, despite this progress, far too many suffer from DKA. Our findings suggest that the US healthcare system fails many emerging adults with diabetes, and that improving the pediatric-to-adult medical transition is imperative.[4] They also carry broader implications: reforms of the healthcare system—including achieving universal coverage, eliminating financial barriers to care and medications, and improving continuity of care—might reduce the toll not only of DKA, but the complications of other chronic, yet thankfully now manageable, conditions.

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Compliance with Ethical Standards:

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