

# Recent Trends in Hospitalization for Diabetic Ketoacidosis in Ontario Children

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**OBJECTIVE** — To investigate trends and geographic variation in diabetic ketoacidosis (DKA) hospitalization rates among children in Ontario from 1991 to 1999.

**RESEARCH DESIGN AND METHODS** — Canadian Institute for Health Information (CIHI) data were used to identify 15,872 diabetes-related hospital admissions in children younger than 19 years in Ontario from 1991 to 1999. Of these, 5,008 admissions were because of DKA and 10,864 admissions were because of conditions other than DKA (non-DKA). Small area variation analysis was used to compare areas with high versus low DKA admission rates.

**RESULTS** — There was a 19% relative decrease in the overall diabetes admission rate over the study period. Non-DKA admissions decreased by 29%, whereas DKA admissions remained stable. Total days of care decreased by 393 days per year for non-DKA admissions and by 99 days per year for DKA admissions. The average length of hospital stay decreased from 4.9 to 3.5 days for non-DKA admissions and from 4.5 to 3.2 days for DKA admissions. The fatality rate was 0.19% for non-DKA admissions and 0.18% for DKA admissions. Variation across geographic areas remained stable for DKA over the study period (Kendall's correlation coefficient 0.64,  $P = 0.017$ ) with an average 3.7-fold difference between the lowest and highest regions.

**CONCLUSIONS** — Increased ambulatory care efforts for children with type 1 diabetes in Ontario have successfully reduced non-DKA admission rates. However, DKA admission rates have remained stable. Geographic variation for DKA admissions is low, but the observed 3.7-fold difference is clinically important for a preventable complication with a significant potential for long-term morbidity and mortality. Prevention strategies are needed, particularly in areas identified with the highest rates.

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**P**rior to the discovery of insulin in 1921, children with type 1 diabetes inevitably died of diabetic ketoacidosis (DKA). Despite major advances in the care of diabetes, DKA remains a leading cause of hospitalization and the leading cause of death and morbidity in children and adolescents with type 1 dia-

betes (1,2). Most DKA-related mortality and morbidity arise as a consequence of development of cerebral edema, an incompletely understood complication of DKA and/or its management (3–5). There is little information on hospitalization trends for DKA in children and adolescents at the population level. In the Neth-

erlands, despite a significant decrease in overall diabetes admissions between 1980 and 1991, DKA admissions in children increased (6). This trend is concerning given the increase in the prevalence of type 1 diabetes in youth worldwide (7,8).

During the 1990s in the Province of Ontario, Canada, there was an overall trend of fewer pediatric inpatient admissions for both medical and surgical conditions (9). The objectives of this study were 1) to examine trends in hospitalization for diabetes and DKA in children in Ontario during the period from 1991 to 1999 and 2) to assess whether geographic variations in DKA hospitalization rates exist across the province.

## RESEARCH DESIGN AND METHODS

Hospital admission data were obtained from the Canadian Institute for Health Information (CIHI) hospital discharge database. In Ontario, it is mandatory for all hospitals (including acute and chronic care hospitals and acute psychiatric hospitals) to submit discharge data that describe all inpatient hospital services to CIHI. Information obtained from the database includes primary and secondary discharge diagnosis codes of the International Classification of Diseases, 9th Revision (ICD-9), up to 16 fields, and length of hospital stay, as well as demographic data such as age, sex, and residence code. The Institute for Clinical Evaluative Sciences (ICES), an independent, nonprofit organization that conducts health services research in Ontario, routinely uses the CIHI database. Researchers at the ICES have reported that <1% of records in the CIHI database are missing demographic information (10). Rates of agreement from reabstraction studies are >95% for demographic data and range from 75 to 96% for most responsible diagnosis codes (10).

Data on all patients younger than 19 years with ICD-9 discharge codes 250.0–250.9 during the period of 1 April 1991 to 31 March 2000 (fiscal years 1991–1999) were studied (11). Hospitalization for DKA was defined by ICD-9 discharge codes 250.1–250.3. Diabetes admissions not due to DKA (non-DKA) were defined

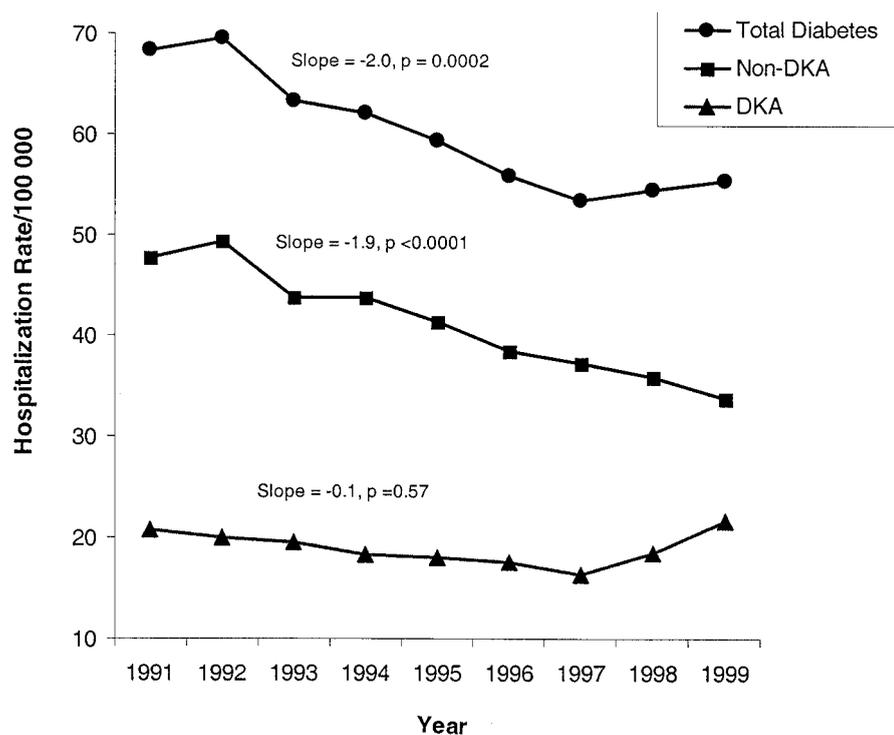
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**Abbreviations:** CF, case fatality; CIHI, Canadian Institute for Health Information; DHC, District Health Council; DKA, diabetic ketoacidosis; ICD-9, International Classification of Diseases, 9th Revision; ICES, Institute for Clinical Evaluative Sciences.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.



**Figure 1**—Age- and sex-adjusted total diabetes, DKA, and non-DKA hospitalization rates per 100,000 children aged 0–19 years in Ontario for 1997–1999.

by ICD-9 discharge codes 250.0 or 250.4–250.9. Age trends were evaluated for the following groups: infants and preschool (1–4 years), school age (5–9 years), early adolescent (10–14 years), and late adolescent (15–19 years). Age- and sex-adjusted annual rates were calculated per 100,000 children based on the 1991 and 1996 Canada Census population data and the postcensal estimates. The average length of stay was calculated by dividing the total number of hospitalization days by the number of admissions. Linear regression was used to assess the increasing or decreasing trend of admission rates over time. The estimated slope from the regression model with a  $P$  value  $< 5\%$  was considered statistically significant.

Geographic variation in admission rates was described using the extremal quotient (EQ): the ratio of highest to lowest rates (12). Admission rates were reported by the patient's District Health Council (DHC) area of residence as determined by the residence codes. DHCs are local health planning and advisory organizations that report to the province's Ministry of Health and Long-Term Care. All rates were adjusted for age and sex and were reported for 3-year intervals to en-

sure stability of rates. Kendall's  $W$  was calculated to assess stability of admission ranking by geographic area over the three study intervals. The Spearman correlation coefficient was used to assess the association between DKA and non-DKA admission ranking within geographic areas during a single time period.

Because the accuracy of data for diagnostic codes from the CIHI database is disease-specific, we conducted an audit of all diabetes admissions during the period of 1997–1998 from four major pediatric centers across Canada. Criteria for the diagnosis of DKA was defined as any child with a venous blood gas pH  $< 7.3$  and/or a serum bicarbonate level  $< 15$  mmol/l in the presence of hyperglycemia and ketonuria. These criteria were compared with the ICD-9 discharge codes for a diagnosis of DKA (250.1–250.3). The sensitivity and specificity of the ICD-9 DKA codes were 68 and 92%, respectively, indicating an overall coding accuracy of 83%.

**RESULTS**— The CIHI database identified a total of 15,872 diabetes-related admissions in children younger than 19 years in Ontario during the fiscal period from 1991 to 1999. Of these, 5,008 admissions were because of DKA and

10,864 admissions were because of non-DKA conditions. Of the DKA cases, the ICD-9 code was 250.1 (diabetes with ketoacidosis) in 96%, 250.2 (hyperosmolar coma) in 1.9%, and 250.3 (diabetic coma) in 1.7%. Diabetes without mention of complication (ICD-9 code 250.0) was the primary diagnosis code in 49% of the non-DKA cases. The next most common primary diagnoses for non-DKA cases included gastroenteritis or abdominal pain (5.7%), diabetes with peripheral circulatory disorders (4.2%), diabetes with unspecified complication (2.5%), and disturbances in tooth eruption (1.1%).

Figure 1 shows the overall hospital admission rates for total diabetes, non-DKA, and DKA hospitalizations. The total diabetes (i.e., DKA + non-DKA) hospitalization rate for children decreased from 68.36 per 100,000 in 1991 to 55.4 per 100,000 in 1999 (relative decrease 19%, slope  $-2.0$ ,  $P = 0.0002$ ). There was a steady 29% decrease in non-DKA admissions over the 1991–1999 period (slope  $-1.9$ ,  $P < 0.001$ ) and no significant change in DKA admissions (slope  $-0.13$ ,  $P = 0.58$ ). There was a 10.4% decrease in DKA admissions from 1991 to 1997 (slope  $= -0.7$ ,  $P < 0.001$ ), with an increase back to 1991 rates after 1998.

Table 1 shows the age- and sex-adjusted hospital admission rate per 100,000 population and the absolute number of admissions due to diabetes and DKA per year according to age group. Over the study period, total diabetes admissions decreased in all age categories except for the 0- to 4-year age group, which showed a 26% increase (slope 0.81,  $P = 0.012$ ). The 15- to 19-year age group showed the greatest decrease (27%: slope  $-4.8$ ,  $P < 0.001$ ). There were no significant changes in DKA admissions among the 5- to 9-year, 10- to 14-year, and 15- to 19-year age groups. In contrast, there was a 220% increase in DKA admissions among the 0- to 4-year age group (slope 0.42,  $P = 0.04$ ).

Figure 2 demonstrates that total days of hospital care decreased by  $\sim 393$  days per year for total diabetes admissions ( $P < 0.0001$ ) and by 99 days per year for DKA admissions ( $P = 0.008$ ). There was a small but significant decrease in the average lengths of stay for both groups, from 4.9 to 3.5 days (slope  $-0.18$ ,  $P < 0.001$ ) for non-DKA admissions and from 4.5 to 3.2 days (slope  $-0.18$ ,  $P = 0.0001$ ) for DKA admissions.

**Table 1—Sex-adjusted total diabetes and DKA hospitalization rates per 100,000 and absolute number of admissions by age group from 1991 to 1999**

	0–4 years		5–9 years		10–14 years		15–19 years		0–19 years	
	Total diabetes	DKA	Total diabetes	DKA	Total diabetes	DKA	Total diabetes	DKA	Total diabetes	DKA
1991	22.4 (164)	2.7 (20)	47.5 (333)	7.8 (55)	85.6 (571)	28.2 (175)	120.2 (852)	46.7 (331)	68.4 (1,920)	20.7 (581)
1992	21.1 (158)	3.8 (28)	53.3 (382)	8.8 (83)	86.6 (590)	23.5 (180)	120.8 (850)	45.5 (320)	69.5 (1,980)	20.1 (571)
1993	20.2 (153)	4.0 (30)	44.2 (320)	7.0 (51)	83.3 (580)	25.0 (174)	110.0 (769)	44.0 (308)	63.3 (1,822)	19.6 (563)
1994	21.6 (164)	3.7 (28)	41.2 (303)	5.4 (40)	83.9 (597)	26.7 (190)	105.6 (747)	39.2 (276)	82.2 (1,811)	18.3 (534)
1995	23.2 (176)	6.2 (47)	40.5 (303)	7.5 (56)	75.2 (546)	23.0 (167)	101.5 (722)	36.8 (262)	59.4 (1,747)	18.1 (532)
1996	21.3 (161)	4.4 (33)	38.8 (295)	7.4 (56)	75.4 (558)	23.1 (171)	90.4 (652)	36.3 (262)	55.9 (1,666)	17.5 (522)
1997	23.6 (175)	5.5 (41)	39.3 (304)	8.6 (67)	63.9 (481)	18.0 (135)	88.5 (646)	33.8 (247)	53.5 (1,608)	16.3 (490)
1998	27.7 (201)	8.3 (60)	40.0 (307)	8.1 (64)	63.1 (480)	21.3 (162)	88.4 (656)	36.8 (273)	54.5 (1,644)	18.5 (559)
1999	28.2 (200)	8.7 (62)	37.2 (295)	7.4 (59)	67.5 (519)	26.4 (203)	87.8 (662)	44.0 (332)	55.4 (1,676)	21.7 (656)
Slope	0.81	0.68	−1.6	0.02	−3.2	−0.39	−4.8	−1.0	−2.0	−0.13
SEM	0.24	0.13	0.38	0.14	0.49	0.36	0.5	0.58	0.29	0.22
P	0.01	0.0012	0.004	0.86	0.0004	0.31	<0.0001	0.1	0.0002	0.57

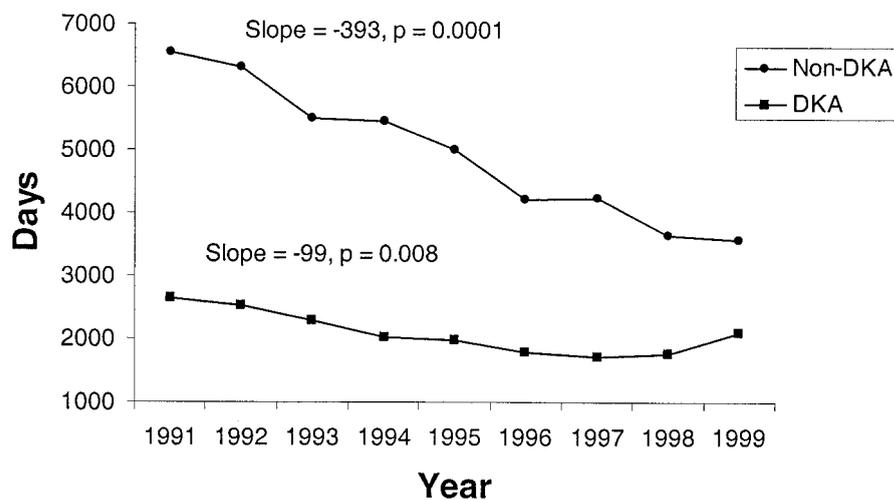
Data are sex-adjusted hospital rates per 100,000 population (absolute number of admissions). Slope, SEM, and P values were determined by linear regression analysis.

The decrease in total diabetes admissions was greater for girls than for boys ( $P < 0.001$ ). There were no significant differences in trends between sexes for DKA admissions. There were 9 deaths among the 5,008 DKA cases, making the case fatality rate for Ontario 0.18% over the 1991–1999 time period. There were 21 deaths among the 10,864 non-DKA admissions (case fatality 0.19%). The primary admitting diagnostic categories for the non-DKA deaths included cystic fibrosis (six cases), infection (five cases), congenital heart disease (four cases), malignancy (two cases), psychiatric disturbance (one case), immune deficiency (one case), epilepsy (one case), and cholangitis (one case).

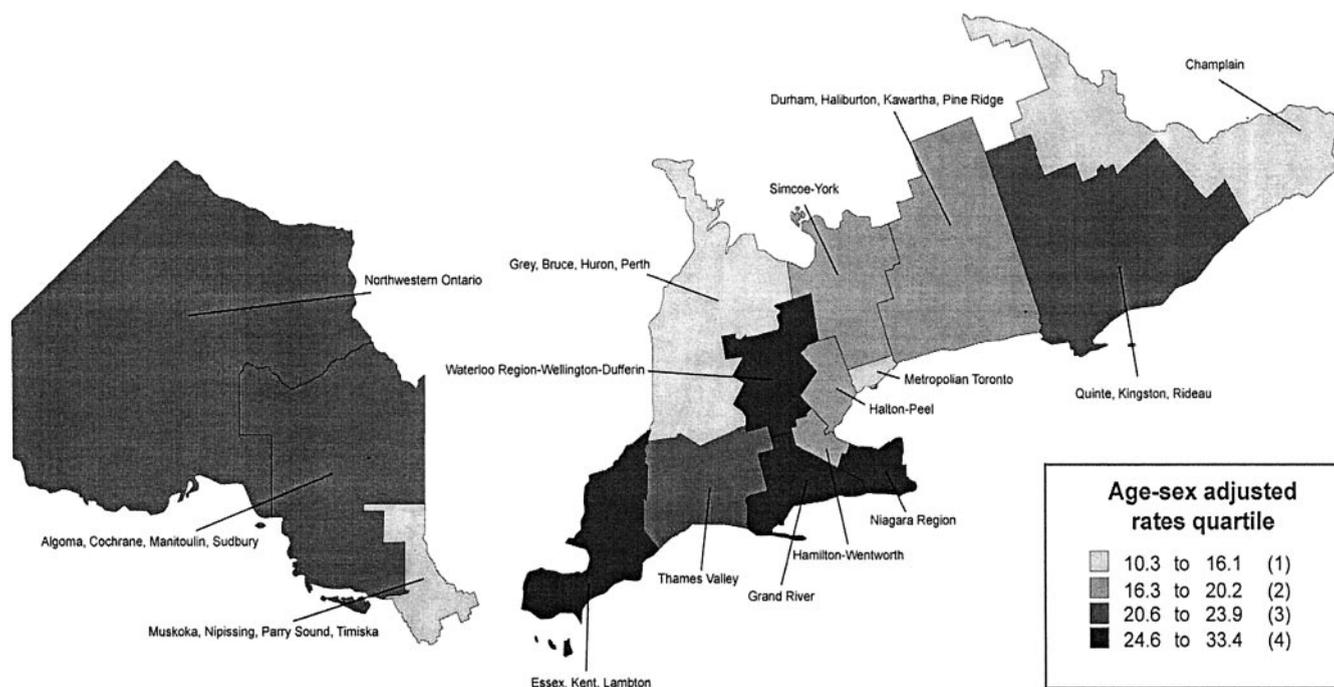
Small area variation analysis examining geographic variation in DKA and non-DKA admission rates was performed for 3-year time intervals. The extremal quotient (ratio of highest to lowest admission rates) for DKA was 4.3, 3.5, and 3.2 for the periods of 1991–1993, 1994–1996, and 1997–1999, respectively, with an average of 3.7 over the study period. The extremal quotients were slightly lower for

the non-DKA admissions: 2.5, 3.1, and 2.7 for the periods of 1991–1993, 1994–1996, and 1997–1999, respectively, with an average of 2.8 over the study period. Results of the DKA admission small area variation analysis for the period from

1997 to 1999 are shown in the map of Ontario in Fig. 3. There are no academic pediatric centers located in the four DHC regions in the highest admission rate quartile. The Toronto DHC consistently had the lowest rates for 1991–1993,



**Figure 2—Total days of care for DKA and non-DKA hospitalizations for Ontario children aged 0–19 years (1997–1999).**



**Figure 3**—Age- and sex-adjusted DKA hospitalization rates per 100,000 children aged 0–19 years by DHC area of patient residence in Ontario (1997–1999).

1994–1996, and 1997–1999 (10, 9.7, and 10.3 per 100,000, respectively). This trend was also seen for non-DKA admission rates. The relative ranking of DKA and non-DKA admission rates for a geographic area remained stable over the three time periods studied ( $W = 0.64$ ,  $P = 0.017$  and  $W = 0.86$ ,  $P = 0.001$ , respectively). The relative ranking of DKA admissions was similar to the relative ranking of non-DKA admissions for a geographic area for the 1991–1993 and 1994–1996 time periods ( $\rho = 0.52$ ,  $P = 0.04$  and  $\rho = 0.75$ ,  $P = 0.001$ , respectively). There was no significant correlation between the DKA and non-DKA admissions area relative ranking during the 1997–1999 period.

**CONCLUSIONS**— There was a significant decrease in total diabetes admissions in Ontario children over the study period from 1991 to 1999. During this period, decreases in pediatric hospital admissions also occurred for overall medical admissions (by 37%) as well as for other disease-specific conditions such as asthma and gastroenteritis (by 32 and 30%, respectively) (9). The decrease in total diabetes admissions was due to decreases in non-DKA-related admissions. This likely resulted, largely in part, from

increased use of ambulatory care strategies in Ontario for children with new-onset diabetes. In 1988–1989, all 83 children presenting with new-onset diabetes to the Hospital for Sick Children in Toronto were admitted for an average of 7.8 days. By 1995–1996, only 27 of 92 children with new-onset diabetes were admitted and for an average of only 2.8 days, whereas the remaining 71% received ambulatory care (13). This trend has important implications in terms of health care cost reduction. Two studies from the U.S. reported that the average cost of a 3- to 5-day diabetes hospital stay was \$2,500–3,000 (U.S.) per patient, with a reduction to \$550–625 (U.S.) per patient for outpatient management (14,15). This represents a potential cost saving of ~80%. Outpatient management of children with new-onset diabetes has been demonstrated to be equivalent to or better than inpatient care in other diabetes-specific outcome measures, including hospital readmission rates, HbA<sub>1c</sub>, and frequency of hypoglycemia and DKA (16–24). A randomized controlled trial comparing hospital and home care in 63 children with new-onset type 1 diabetes found that the group that received home care had a 0.6–0.7% lower HbA<sub>1c</sub> at 24 and 36 months after diagnosis (24). Swift

et al. (17) demonstrated that children who received initial home diabetes management had 19% less diabetes-related hospital readmissions than those who received hospital-based care.

In contrast to non-DKA admissions, the DKA admission rate was relatively stable over the study period. However, it is important that increased ambulatory care strategies have not resulted in an increase in DKA admissions. Although the CIHI data do not discriminate the point in the course of diabetes at which the episode of DKA occurred, it is likely that most occur at initial presentation of diabetes. Our ICD-9 coding audit revealed that during 1997, 84% of DKA admissions at the Hospital for Sick Children in Toronto occurred in children presenting with new-onset diabetes. Of concern is the dramatic 220% increase in DKA admissions observed in the 0- to 4-year age group. In a recent study of incidence trends in childhood diabetes across Europe, the 0- to 4-year age group displayed the highest annual increase (4.8%) (25). Whether it is sufficient to explain the DKA admission increase in Ontario is unclear. Our findings do, however, highlight the need for increased vigilance for the early presenting symptoms of diabetes in this vulnerable age group.

Two population-based hospitalization studies utilizing similar ICD-9 diagnostic criteria in children with diabetes from California and the Netherlands are available for comparison (6,26). The incidence of type 1 diabetes in North American children is ~1.5–2 fold higher than that in children from the Netherlands (6,27–29). DKA-specific admission rates are higher than expected based on incidence factors alone in Ontario and California in comparison to the Netherlands (20.1 vs. 19.0 vs. 3.4 per 100,000 respectively). Total diabetes admissions are higher in Ontario than in both California and the Netherlands (68.4 vs. 31.9 vs. 25.2 per 100,000 respectively). The average length of stay was substantially less for Ontario children compared to children from the Netherlands (5 vs. 14.5 days respectively). Differences in length of stay are largely due to differences in patterns of hospitalization for newly diagnosed diabetes (6).

The Ontario DKA case fatality (CF) estimate of 0.18% is slightly lower than that reported from a study using a U.S. national tertiary pediatric hospital database during the 1980s (CF 0.25%) and from the more recent study by Glaser et al. (30) which involved tertiary U.S. pediatric centers (CF 0.21%) (4). It is reassuring that the Ontario estimate, which includes hospitals at all levels of care, is in keeping with estimates reported from major pediatric centers. Most non-DKA deaths seem to have occurred among children with diabetes secondary to conditions such as cystic fibrosis or drugs rather than type 1 diabetes. Although the ICD-9 hospital discharge codes do not discriminate between diabetes type, it is likely that most non-DKA admissions were due to type 1 diabetes, as evidenced by the most common primary discharge codes (i.e., diabetes without mention of complication and gastroenteritis); the secondary causes of diabetes were overrepresented among the deaths.

Analysis of small area variation in health outcomes may facilitate both health care resource allocation and prevention strategies in areas of greatest perceived need. In our study, geographic variation for DKA was similar to other pediatric conditions in Ontario, such as asthma and gastroenteritis, which have three- and fivefold regional differences, respectively (31). The differences observed for DKA are clinically important,

given that it is a preventable condition associated with significant risk for morbidity and mortality. In general, the more populated urban areas had lower rates of both DKA and non-DKA admissions compared with the more remote sparsely populated regions. For example, the Metropolitan Toronto DHC had the lowest admission rates for all three time periods studied. This large urban area likely provides greater access to both primary and tertiary care than more remote regions.

Recent data suggest that simple community interventions may prevent or reduce the incidence of DKA at the time of diagnosis of diabetes. In a program in Parma, Italy, schools and doctors' offices were provided with colorful posters with practical messages about diabetes, and local pediatricians were instructed on the use of glucose meters (32). In the study area, the incidence of DKA in new-onset cases decreased from 78% in 1987–1991 to 12.5% in 1991–1997; no cases were reported in the last 4 years of the study. In the control region nearby, in which the intervention was not performed, 83% of new cases presented in DKA.

DKA in established diabetes is most often due to inappropriate management of intercurrent illness or deliberate omission of insulin (33–35). At least two studies document the effectiveness of patient education and the availability of advice via a 24-h telephone hotline in reducing the incidence of DKA associated with intercurrent illness (33, 34). Omission of insulin may also be preventable with a hierarchical set of educational, supervisory, and psychosocial interventions aimed at determining the reason for the omission of insulin and preventing its recurrence (35).

The hospitalization data from CIHI rely on the quality of the administrative hospital discharge data. The results of our audit from four large tertiary pediatric centers across Canada indicated an overall accuracy of 83% between the CIHI database discharge codes and expert criteria for diagnosis of DKA. The level of agreement was higher than that reported in Canadian studies for a diagnosis of Guillain-Barré syndrome, asthma, rheumatoid arthritis, or stroke and in keeping with levels of agreement for acute myocardial infarction and diabetes (10,36–43). However, our reabstraction study included only large tertiary pediatric care facilities, and whether these results are

generalizable to other centers is not known. Another limitation of the database is the lack of individual patient detail, such as timing of DKA in relation to onset of diabetes, severity of the DKA episode, and long-term outcomes other than death. Despite these limitations, the CIHI database remains the most reliable and feasible means of assessing health care utilization for large populations in Canada.

In summary, increased ambulatory care strategies have been successful in decreasing non-DKA-related hospital admissions for Ontario children. DKA admission rates have been relatively stable since 1992. The reason for the observed geographic variation in DKA admissions requires further evaluation so prevention strategies can be targeted to the areas with greatest need.

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