# Rates of Diabetic Ketoacidosis: International Comparison With 49,859 Pediatric Patients With Type 1 Diabetes From England, Wales, the U.S., Austria, and Germany

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## OBJECTIVE

**Diabetic ketoacidosis (DKA) in children and adolescents with established type 1 diabetes is a major problem with considerable morbidity, mortality, and associated costs to patients, families, and health care systems. We analyzed data from three multinational type 1 diabetes registries/audits with similarly advanced, yet differing, health care systems with an aim to identify factors associated with DKA admissions.**

## RESEARCH DESIGN AND METHODS

**Data from 49,859 individuals <18 years with type 1 diabetes duration ≥1 year from the Prospective Diabetes Follow-up Registry (DPV) initiative (*n* = 22,397, Austria and Germany), the National Paediatric Diabetes Audit (NPDA; *n* = 16,314, England and Wales), and the T1D Exchange (T1DX; *n* = 11,148, U.S.) were included. DKA was defined as ≥1 hospitalization for hyperglycemia with a pH <7.3 during the prior year. Data were analyzed using multivariable logistic regression models.**

## RESULTS

**The frequency of DKA was 5.0% in DPV, 6.4% in NPDA, and 7.1% in T1DX, with differences persisting after demographic adjustment ($P < 0.0001$). In multivariable analyses, higher odds of DKA were found in females (odds ratio [OR] 1.23, 99% CI 1.10–1.37), ethnic minorities (OR 1.27, 99% CI 1.11–1.44), and $HbA_{1c}$ ≥7.5% (≥58 mmol/mol) (OR 2.54, 99% CI 2.09–3.09 for $HbA_{1c}$ from 7.5 to <9% [58 to <75 mmol/mol] and OR 8.74, 99% CI 7.18–10.63 for $HbA_{1c}$ ≥9.0% [≥75 mmol/mol]).**

## CONCLUSIONS

**These multinational data demonstrate high rates of DKA in childhood type 1 diabetes across three registries/audits and five nations. Females, ethnic minorities, and $HbA_{1c}$ above target were all associated with an increased risk of DKA. Targeted DKA prevention programs could result in substantial health care cost reduction and reduced patient morbidity and mortality.**


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In children and adolescents, diabetic ketoacidosis (DKA) represents the most serious acute complication of type 1 diabetes, which usually results in admission to the hospital and is associated with a 0.15–0.3% mortality rate (1–4). DKA not only has considerable costs to health care systems (5) but there is also an added burden of cost to patients and their families. In 2004–2009 in the U.S., the mean hospital cost per pediatric DKA admission was $7,142 (range $4,125–11,916) (6), and insurance claims data from 2007 reported an excess of $5,837 in annual medical expenditures for youth with insulin-treated diabetes with DKA compared with those without DKA (7). In Germany, pediatric patients with diabetes with DKA had diabetes-related costs that were up to 3.6-fold higher compared with those without DKA (8).

Rates of DKA in youth with type 1 diabetes vary widely nationally and internationally, from 15% to 70% at diagnosis (4) to 1% to 15% per established patient per year (9–11). However, data from systematic comparisons between countries are limited. To address this gap in the literature, we analyzed registry and audit data from three organizations: the Prospective Diabetes Follow-up Registry (DPV) in Germany and Austria, the National Paediatric Diabetes Audit (NPDA) in England and Wales, and the T1D Exchange (T1DX) in the U.S. These countries have similarly advanced, yet differing, health care systems in which data on DKA and associated factors are collected. Our goal was to identify indicators of risk for DKA admissions in pediatric patients with >1-year duration of disease with an aim to better understand where targeted preventive programs might lead to a reduction in the frequency of this complication of management of type 1 diabetes.

## RESEARCH DESIGN AND METHODS

### Participants

#### *DPV*

The DPV registry is a prospective longitudinal standardized computer-based documentation system for patients with all diabetes types. All children <18 years old with type 1 diabetes duration ≥1 year ($n$ = 22,397) who had at least one office visit in 2011 or 2012 were included in this report from the 281 sites. Currently, more than 90% of German and more than 70% of Austrian children with diabetes are included in the registry. Data are documented locally by the participating centers in an electronic health record. Twice yearly, anonymized data are exported and transmitted for central analyses. Missing and inconsistent data are reported back to the centers for correction. Data collection is approved by the ethics committee at Ulm University and by the institutional review boards (IRBs) at the participating centers (12,13), which are listed in the Supplementary Data.

#### *NPDA*

The NPDA collects data on outcomes and care processes for children and young people diagnosed with diabetes who attend pediatric diabetes units (PDUs) where diabetes care is provided in England and Wales (http://www.rcpch.ac.uk/npda). Each PDU submits data annually to the NPDA. Data for this report were collected between 1 April 2011 and 31 March 2012 and include all children <18 years old with a diagnosis of type 1 diabetes for at least 1 year attending a PDU ($n$ = 16,314). A total of 177 PDUs from England and Wales submitted data for this time period. Information about DKA admissions was obtained by linkage of unique patient identifiers submitted to the NPDA with the Hospital Episode Statistics (England) and the Patient Episode Database for Wales (Wales). These two databases collect information on all hospital admissions in England and Wales, with ICD classification being used to code the data. The Royal College of Paediatrics and Child Health, which delivers the NPDA, has approval to collect and hold patient information for the NPDA without written consent. However, patients and their parents are informed of the submission of their data to the NPDA by the local PDU.

#### *T1DX*

The T1DX Clinic Network includes 75 U.S.-based pediatric and adult endocrinology practices. A registry of more than 26,000 individuals with type 1 diabetes commenced enrollment in September 2010 (14). Each clinic received approval from a local IRB. Informed consent was obtained according to IRB requirements. Data were collected for the registry's central database from the participant's medical record and by having the participant or the participant's parent complete a comprehensive questionnaire, as previously described (14). Method of insulin delivery (pump/injection), age, type 1 diabetes duration, race/ethnicity, $HbA_{1c}$, height, weight, and frequency of DKA were extracted from the medical record. This analysis included 11,148 youth aged <18 years old with a type 1 diabetes duration ≥1 year enrolled between September 2010 and August 2012 at 1 of the 52 registry sites caring for pediatric patients. The participating centers are listed in the Supplementary Data.

### Outcome Measures

DKA (≥1 episode in the prior year) was defined in all the countries using similar criteria, which included:

- arterial, venous, or capillary pH of less than 7.30 and/or serum bicarbonate of less than 15 mmol/L, and
- treatment provided in a health care facility.

The T1DX definition required two additional criteria:

- symptoms such as polyuria, polydipsia, nausea, or vomiting, and
- elevated serum ketone levels or large/moderate urine ketones.

#### *Explanatory Variables*

Median $HbA_{1c}$ over the year of the registry assessment was used to represent $HbA_{1c}$ in this analysis. For all registries/audits, all $HbA_{1c}$ values were Diabetes Control and Complications Trial (DCCT)-standardized (15). Any use of a pump during the observation period was categorized as pump use; otherwise, patients were categorized as using injections. For all registries, BMI $z$ score was calculated from height and weight and adjusted for age and sex, using World Health Organization (WHO) reference tables (16,17).

Ethnic minority status for DPV was defined as at least one parent born outside of Germany or Austria (positive migration history). Ethnicity data for England and Wales was reported to the NPDA by the participating center. This is a self-reported ethnicity by the patient and the patient's family using a list of contemporary ethnic categories (white, black, Asian, mixed, other, or not stated). Minority status was defined as nonwhite, with "not stated" being excluded as missing data. For the T1DX,

ethnic minority status was defined as other than non-Hispanic white.

### Statistical Methods

Summary statistics were calculated within registries/audits and are given as the median with quartiles for continuous variables and as the percentage for dichotomous variables. Kruskal-Wallis or $\chi^2$ tests were performed to compare basic demographic and clinical characteristics among registries/audits. The proportions of participants with at least one DKA event in the past 12 months were tabulated by registries/audits and by strata of each explanatory variable. Next, unadjusted odds of DKA were calculated by registry/audit and overall for the following potential indicators of greater risk for DKA: age (<6 years, 6 to <13 years, 13 to <18 years), sex, type 1 diabetes duration (1 to <3 years, ≥3 years), $HbA_{1c}$ (<7.5% [<58 mmol/mol], 7.5 to 9.0% [58 to <75 mmol/mol], ≥9.0% [≥75 mmol/mol]), pump versus injection, BMI *z* score (underweight [<5th percentile], normal weight [5th–85th percentile], overweight [85th–95th percentile], obesity [>95th percentile]) defined according to WHO cutoffs for age and sex, and ethnic minority status (yes/no). These analyses were repeated with multivariable models to compare DKA rates between the registries/audits. A stepwise approach was used to adjust logistic regression models for age-group, sex, type 1 diabetes duration group, ethnicity, $HbA_{1c}$ group, BMI category, and pump use. Additional analyses were performed stratified by age-groups. All statistical analyses were performed using SAS 9.4 software (SAS Institute, Inc., Cary, NC). All *P* values are two-sided. A priori, in view of the large sample size and multiple comparisons, only *P* values <0.01 were considered statistically significant.

## RESULTS

Patient characteristics (Table 1) were similar across the three registries/audits for sex. Due to the large sample size, differences in age, age at diagnosis, and duration of type 1 diabetes were statistically significant, but these small differences were not clinically important. DPV and T1DX had higher rates of pump use (44.2% and 56.1%, respectively) compared with NPDA (11.5%). Ethnic minority status ranged from 22.6% in T1DX to 20.4% in DPV and to 10.4% in NPDA. Mean $HbA_{1c}$ was lowest in DPV (63 mmol/mol [7.9%]), intermediate in T1DX (69 mmol/mol [8.5%]), and highest in NPDA (75 mmol/mol [9.0%]). As reported in Table 1, the proportion of subjects with at least one DKA event in the prior year was lowest in DPV (5.0%), intermediate in NPDA (6.4%), and highest in T1DX (7.1%).

In univariate analyses (Table 2) of variables associated with DKA in the combined population of 49,859 pediatric patients with type 1 diabetes, the following variables were associated with higher rates of DKA: age 13 to <18 years compared with <6 years (odds ratio [OR] 1.54, 99% CI 1.20–1.97), female sex (OR 1.35, 99% CI 1.23–1.49), type 1 diabetes duration >3 years (OR 1.37, 99% CI 1.21–1.53), minority status (OR 1.44, 99% CI 1.28–1.62), and $HbA_{1c}$ (7.5% to <9% [58–75 mmol/mol], OR 2.40, 99% CI 1.99–2.90, and ≥9% [75 mmol/mol], OR 8.04, 99% CI 6.72–9.62). DKA frequency was lower in pump users than in injection users (OR 0.84, 99% CI 0.76–0.93). Heterogeneity in the association with DKA between registries was seen for pump use and age category, and the overall rate should be interpreted accordingly. A lower rate of DKA in pump users was only found in T1DX, in contrast to no association of pump use with DKA in DPV or NPDA. A higher rate of DKA in the 13- to <18-year-old group was seen in NPDA but was not statistically significant in DPV or T1DX. Similar associations for sex, type 1 diabetes duration, and minority status were seen across registries/audits.

In multivariable analyses (Table 3), age, type 1 diabetes duration, and pump use were not significantly associated with DKA in the fully adjusted model. Females had 23% higher odds of DKA than males (OR 1.23, 99% CI 1.10–1.37), and country-specific ethnic minorities had 27% higher odds than nonethnic minorities (OR 1.27, 99% CI 1.11–1.44). The highest odds for DKA were among those with elevated $HbA_{1c}$, with an OR of 2.54 (99% CI 2.09–3.09) for $HbA_{1c}$ 7.5 to <9% and an OR of 8.74 (99% CI 7.18–10.63) for $HbA_{1c}$ ≥9.0% (75 mmol/mol). Once $HbA_{1c}$ was included (models 4 and 5), the registry/audit-specific variable was not associated with DKA for T1DX but was inversely associated with DKA

**Table 1—Descriptive data by registry**

| | Overall *N* = 49,859 | DPV *n* = 22,397 | NPDA *n* = 16,314 | T1DX *n* = 11,148 | *P* value |
|---|---|---|---|---|---|
| Male | 52.2 | 52.2 | 53.0 | 51.1 | 0.013 |
| Age, years | 13.3 (10.3, 15.7) | 13.8 (10.5, 16.3) | 13.2 (10.4, 15.3) | 12.7 (9.8, 15.2) | <0.001 |
| Age at diagnosis, years | 6.9 (3.9, 10.0) | 7.1 (4.0, 10.4) | 7.1 (3.9, 10.2) | 6.0 (3.0, 9.0) | <0.001 |
| Type 1 diabetes duration, years | 4.9 (2.7, 7.8) | 5.0 (2.9, 8.1) | 4.7 (2.6, 7.5) | 4.0 (2.0, 7.0) | <0.001 |
| BMI *z* score, WHO | 0.72 (0.08, 1.40) | 0.65 (0.02, 1.30) | 0.81 (0.13, 1.52) | 0.79 (0.16, 1.48) | <0.001 |
| Pump use | 36.1 | 44.2 | 11.5 | 56.1 | <0.001 |
| Ethnic minority | 18.0 | 20.4 | 10.4 | 22.6 | <0.001 |
| Mean $HbA_{1c}$ | | | | | |
| % | 8.4 ± 1.5 | 7.9 ± 1.4 | 9.0 ± 1.6 | 8.5 ± 1.4 | <0.001 |
| mmol/mol | 68 ± 16 | 63 ± 15 | 75 ± 17 | 69 ± 15 | |
| $HbA_{1c}$ | | | | | |
| <58 mmol/L (7.5%) | 28.3 | 42.9 | 12.0 | 20.9 | <0.001 |
| ≥75 mmol/mol (9%) | 27.2 | 16.9 | 42.0 | 28.0 | <0.001 |
| With ≥1 DKA event | 6.0 | 5.0 | 6.4 | 7.1 | <0.001 |

Data shown are unadjusted percentages, mean ± SD, or median and quartiles.

**Table 2—DKA rate and unadjusted ORs of DKA by registry with 99% CIs**

| | Overall | | | DPV | | | NPDA | | | T1DX | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *N* | % DKA | OR (99% CI) | *n* | % DKA | OR (99% CI) | *n* | % DKA | OR (99% CI) | *n* | % DKA | OR (99% CI) |
| Age | | | | | | | | | | | | |
| <6 years | 2,693 | 4.5 | 1.00 | 1,171 | 4.3 | 1.00 | 867 | 3.8 | 1.00 | 655 | 6.0 | 1.00 |
| 6 to <13 years | 20,413 | 5.1 | 1.12 (0.87–1.45) | 8,433 | 4.3 | 1.00 (0.67–1.49) | 6,821 | 5.4 | 1.43 (0.89–2.31) | 5,159 | 6.0 | 1.00 (0.64–1.58) |
| 13 to <18 years | 26,753 | 6.8 | 1.54 (1.20–1.97) | 12,793 | 5.6 | 1.34 (0.91–1.96) | 8,626 | 7.6 | 2.07 (1.30–3.31) | 5,334 | 8.4 | 1.44 (0.92–2.25) |
| Sex | | | | | | | | | | | | |
| Male | 26,033 | 5.2 | 1.00 | 11,691 | 4.6 | 1.00 | 8,640 | 5.2 | 1.00 | 5,702 | 6.4 | 1.00 |
| Female | 23,826 | 6.9 | 1.35 (1.23–1.49) | 10,706 | 5.6 | 1.23 (1.05–1.44) | 7,674 | 7.9 | 1.58 (1.33–1.86) | 5,446 | 7.9 | 1.26 (1.04–1.53) |
| Type 1 diabetes duration | | | | | | | | | | | | |
| 1 to <3 years | 13,721 | 4.8 | 1.00 | 5,877 | 4.2 | 1.00 | 4,703 | 5.1 | 1.00 | 3,141 | 5.4 | 1.00 |
| >3 years | 36,138 | 6.4 | 1.37 (1.21–1.53) | 16,520 | 5.4 | 1.29 (1.07–1.56) | 11,611 | 7.0 | 1.40 (1.15–1.70) | 8,007 | 7.8 | 1.48 (1.17–1.86) |
| Minority | | | | | | | | | | | | |
| No | 38,925 | 5.6 | 1.00 | 17,827 | 4.7 | 1.00 | 12,471 | 6.4 | 1.00 | 8,627 | 6.1 | 1.00 |
| Yes | 8,532 | 7.9 | 1.44 (1.28–1.62) | 4,570 | 6.3 | 1.36 (1.13–1.63) | 1,441 | 8.3 | 1.31 (1.01–1.71) | 2,521 | 10.4 | 1.78 (1.45–2.18) |
| $HbA_{1c}$ | | | | | | | | | | | | |
| <7.5% (58 mmol/mol) | 13,485 | 1.8 | 1.00 | 9,407 | 1.7 | 1.00 | 1,760 | 2.0 | 1.00 | 2,318 | 2.1 | 1.00 |
| 7.5 to <9.0% (58–75 mmol/mol) | 21,267 | 4.3 | 2.40 (1.99–2.90) | 8,833 | 4.6 | 2.76 (2.16–3.51) | 6,746 | 3.3 | 1.65 (1.03–2.66) | 5,688 | 4.9 | 2.44 (1.62–3.67) |
| ≥9.0% (75 mmol/mol) | 12,977 | 13.0 | 8.04 (6.72–9.62) | 3,706 | 14.6 | 9.78 (7.72–12.39) | 6,164 | 11.0 | 6.07 (3.86–9.54) | 3,107 | 14.9 | 8.28 (5.57–12.32) |
| BMI | | | | | | | | | | | | |
| Underweight | 279 | 9.0 | 1.61 (0.93–2.77) | 138 | 8.0 | 1.62 (0.72–3.66) | 87 | 10.3 | 1.62 (0.65–4.05) | 54 | 9.3 | 1.47 (0.44–4.95) |
| Normal weight | 27,240 | 5.8 | 1.00 | 14,410 | 5.1 | 1.00 | 6,262 | 6.6 | 1.00 | 6,568 | 6.5 | 1.00 |
| Overweight | 10,660 | 6.2 | 1.07 (0.95–1.21) | 5,135 | 5.2 | 1.03 (0.85–1.25) | 2,828 | 6.3 | 0.94 (0.74–1.19) | 2,697 | 7.8 | 1.22 (0.97–1.53) |
| Obesity | 5,632 | 5.6 | 0.97 (0.82–1.14) | 2,293 | 4.2 | 0.83 (0.62–1.10) | 1,655 | 4.8 | 0.70 (0.51–0.97) | 1,684 | 8.3 | 1.29 (1.00–1.68) |
| Method of insulin delivery | | | | | | | | | | | | |
| Injection | 31,811 | 6.3 | 1.00 | 12,494 | 4.9 | 1.00 | 14,445 | 6.4 | 1.00 | 4,872 | 9.6 | 1.00 |
| Pump | 18,003 | 5.3 | 0.84 (0.76–0.93) | 9,903 | 5.2 | 1.05 (0.90–1.23) | 1,869 | 6.8 | 1.07 (0.83–1.37) | 6,231 | 5.2 | 0.51 (0.42–0.62) |

**Table 3—Adjusted odds of DKA based on logistic regression models: what variables explain the differences in DKA rates between ORs and 99% CIs**

| | Model 1 | Model 2 | Model 3 | Model 4 | Model 5 | Model 6 |
|---|---|---|---|---|---|---|
| Registry/audit | | | | | | |
| T1DX vs. DPV | 1.44 (1.28–1.63)* | 1.49 (1.31–1.68)* | 1.47 (1.30–1.67)* | 1.05 (0.92–1.20) | 1.06 (0.93–1.21) | 1.06 (0.93–1.21) |
| NPDA vs. DPV | 1.30 (1.16–1.46)* | 1.33 (1.18–1.49)* | 1.42 (1.26–1.61)* | 0.79 (0.69–0.89)* | 0.78 (0.68–0.90)* | 0.79 (0.68–0.91)* |
| Age | | | | | | |
| 6 to <13 vs. <6 years | — | 0.99 (0.77–1.28) | 0.94 (0.72–1.22) | 0.93 (0.71–1.22) | 0.91 (0.69–1.20) | 0.91 (0.69–1.20) |
| 13 to <18 vs. <6 years | — | 1.35 (1.04–1.74)* | 1.28 (0.99–1.66) | 0.92 (0.70–1.21) | 0.89 (0.67–1.17) | 0.89 (0.67–1.18) |
| Sex | | | | | | |
| Female vs. male | — | 1.35 (1.22–1.49)* | 1.32 (1.19–1.46)* | 1.26 (1.13–1.40)* | 1.23 (1.11–1.38)* | 1.23 (1.10–1.37)* |
| Type 1 diabetes duration | | | | | | |
| >3 vs. 1 to <3 years | — | 1.28 (1.13–1.44)* | 1.30 (1.14–1.47)* | 1.10 (0.96–1.26) | 1.08 (0.94–1.24) | 1.08 (0.94–1.24) |
| Ethnic minority status | | | | | | |
| Yes vs. no | — | — | 1.49 (1.32–1.68)* | 1.27 (1.12–1.44)* | 1.26 (1.11–1.43)* | 1.27 (1.11–1.44)* |
| $HbA_{1c}$ | | | | | | |
| 7.5 to <9.0% vs. <7.5% | — | — | — | 2.48 (2.04–3.00)* | 2.54 (2.09–3.09)* | 2.54 (2.09–3.09)* |
| ≥9.0% vs. <7.5% | — | — | — | 8.64 (7.14–10.45)* | 8.73 (7.18–10.62)* | 8.74 (7.18–10.63)* |
| BMI | | | | | | |
| Underweight vs. normal weight | — | — | — | — | 1.33 (0.74–2.37) | 1.33 (0.74–2.37) |
| Overweight vs. normal weight | — | — | — | — | 1.03 (0.90–1.17) | 1.02 (0.90–1.17) |
| Obesity vs. normal weight | — | — | — | — | 0.84 (0.71–1.00)* | 0.84 (0.71–1.00)* |
| Method of insulin delivery | | | | | | |
| Pump vs. injection | — | — | — | — | — | 1.02 (0.91–1.15) |

*$P < 0.01$.

for NPDA. This can be explained by the T1DX having the highest rate of DKA but the NPDA having the highest $HbA_{1c}$.

The association of age with DKA was further explored in the fully adjusted models (Table 4). Females had higher odds of DKA in the 6- to <13- and 13- to <18-year-old age-groups, but not in those <6 years old. Minority status was only significantly associated with DKA in the 13- to <18-year-old group, although the odds were similar in all age-groups. The highest odds for DKA were for elevated $HbA_{1c}$, with the 13- to <18-year-old group having the greatest risk. In contrast, pump use was associated with elevated odds of DKA in the <6-year-olds and in the 6- to <13-year-olds but with reduced odds of DKA in the 13- to <18-year-olds.

## CONCLUSIONS

The major finding of these analyses is high rates of pediatric DKA across the three registries, even though DKA events at the time of diagnosis were not included. In the prior 12 months, ~1 in 20 (DPV), 1 in 16 (NPDA), and 1 in 14 (T1DX) pediatric patients with a duration of diabetes ≥1 year were diagnosed with DKA and required treatment in a health care facility. Female sex, ethnic minority status, and elevated $HbA_{1c}$ were consistent indicators of risk for DKA across all three registries. These indicators of increased risk for DKA are similar to previous reports (10,11,18,19), and our rates of DKA are within the range in the pediatric diabetes literature of 1–15% per established patient per year (10,11).

Compared with patients receiving injection therapy, insulin pump use was associated with a lower risk of DKA only in the U.S. in the T1DX, but no difference was seen in the DPV or NPDA. Country-specific factors on the associations of risk factors with DKA require further investigation. For pump use, selection bias may play a role in the U.S. The odds of DKA in pump users was not increased in any registry, which is a marked difference from some (10) but not all historic data (20). When data from all three registries were analyzed together, odds of DKA were increased in pump users <6 and 6 to <13 years of age, but decreased in 13- to <18-year-olds. A more detailed analysis of pump use across these three registries indicates differing patterns by age-group, with the highest pump use in <6-year-olds in the DPV, but higher use in the 13- to <18-year-olds in the T1DX, and the lowest pump use in the NPDA (21).

Although this is the largest data set on pediatric DKA reported, we acknowledge limitations of registry-level data, including that the data are cross-sectional. Ascertainment of data across the registries may differ and could introduce bias. For example, the T1DX registry was more stringent in DKA case definition; however, rates of DKA were still the highest of the three registries. Socioeconomic status may also explain some of the increased risk for DKA, but these data were not available for these transnational comparisons. Also, the health care systems in each country differ and likely contribute to differences in DKA but are beyond the scope of this data set and analysis. Further investigation of the advantages and disadvantages of these health care systems could inform changes to reduce pediatric DKA.

DKA and its associated morbidity and mortality can frequently be prevented by following simple diabetes care self-management, such as monitoring blood glucose and checking urine or blood to identify ketosis early (4). Mortality data

**Table 4—Fully adjusted model by age-groups**

| | Age-group <6 years OR (99% CI) | Age-group 6 to <13 years OR (99% CI) | Age-group 13 to <18 years OR (99% CI) |
|---|---|---|---|
| Registry | | | |
| T1DX vs. DPV | 1.31 (0.69–2.49) | 0.92 (0.74–1.15) | 1.20 (1.01–1.42)* |
| NPDA vs. DPV | 1.29 (0.61–2.74) | 0.77 (0.60–1.00)* | 0.79 (0.66–0.95)* |
| Sex | | | |
| Female vs. male | 0.79 (0.47–1.32) | 1.25 (1.04–1.49)* | 1.28 (1.11–1.48)* |
| Type 1 diabetes duration | | | |
| >3 vs. 1 to <3 years | 0.91 (0.50–1.67) | 1.16 (0.94–1.43) | 1.00 (0.82–1.22) |
| Minority | | | |
| Yes vs. no | 1.18 (0.64–2.17) | 1.24 (1.00–1.53)* | 1.29 (1.09–1.54)* |
| $HbA_{1c}$ | | | |
| 7.5 to <9.0% vs. <7.5% | 1.59 (0.82–3.10) | 2.26 (1.72–2.95)* | 3.54 (2.53–4.96)* |
| ≥9.0% vs. <7.5% | 4.89 (2.20–10.87)* | 6.46 (4.80–8.69)* | 13.71 (9.93–18.94)* |
| BMI | | | |
| Underweight vs. normal weight | 2.58 (0.15–45.57) | 0.86 (0.23–3.29) | 1.46 (0.74–2.85) |
| Overweight vs. normal weight | 1.18 (0.66–2.10) | 1.17 (0.94–1.44) | 0.92 (0.78–1.09) |
| Obesity vs. normal weight | 0.89 (0.42–1.89) | 0.88 (0.67–1.17) | 0.82 (0.66–1.03) |
| Method of insulin delivery | | | |
| Pump vs. injection | 2.12 (1.15–3.90)* | 1.32 (1.08–1.61)* | 0.80 (0.68–0.94)* |

Models adjusted for registry, sex, type 1 diabetes duration, minority status, $HbA_{1c}$ category, BMI category, and pump use. *$P < 0.01$.

have not been collected as part of this analysis. The costs of failing to prevent DKA events are significant and should provide an economic incentive to develop DKA prevention programs, which, in turn, would reduce patient morbidity, mortality, and familial distress. By combining SEARCH for Diabetes in Youth (SEARCH) study type 1 diabetes prevalence data with T1DX DKA annual incidence data, we estimate that the costs of treating DKA reach ~$90 million per year in the U.S., calculated as 179,387 (total number of pediatric patients with type 1 diabetes in U.S. based on SEARCH data in 2010 [22]) × rate of T1DX DKA (7.1%) = an estimated 12,736 pediatric DKA cases in the U.S. × $7,142/DKA hospitalization (6). Moreover, each 10% (or ~1,274 DKA cases) absolute reduction in DKA would result in a potential savings of $9 million/year. Costs for pediatric DKA vary, with some sources reporting higher (19) or lower costs (7), and these data should be considered as estimates of the effect of the economic savings with DKA prevention. It should be noted that these estimates do not include the high costs of treating the devastating long-term sequelae of cerebral edema and other complications that can accompany the treatment of DKA. Thus, cost-effective DKA prevention programs need to be developed and tested for their effectiveness. Such prevention programs in pediatrics should target females, ethnic minorities, and youth with $HbA_{1c}$ levels above target because these groups are at increased risk of developing DKA.

These multicenter data in almost 50,000 children demonstrate many similarities and some important differences in DKA in childhood type 1 diabetes from three registries across five nations. Benchmarking such data is important so countries can better understand where to target interventions to improve quality of care. These analyses highlight the high annual rates of DKA in the pediatric population in these developed Western nations that already have sophisticated and advanced health care systems. These data should serve as a call to action to develop programs to reduce pediatric DKA.

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