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# Presence of Diabetic Ketoacidosis at Diagnosis of Diabetes Mellitus in Youth: The Search for Diabetes in Youth Study

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## What's Known on This Subject

There are few population-based epidemiologic studies on the prevalence and predictors of DKA at onset of type 1 and type 2 diabetes in youth. Prevalence of DKA at diagnosis has not decreased decisively over the past 20 years.

## What This Study Adds

This is the first large US population-based study of DKA at the onset of diabetes. The study ruled out ethnicity as a predictor of DKA and demonstrated that lack of health insurance, low family income, and parental education predict DKA.

## ABSTRACT

**OBJECTIVE.** The purpose of this work was to determine the prevalence and predictors of diabetic ketoacidosis at the diagnosis of diabetes in a large sample of youth from the US population.

**PATIENTS AND METHODS.** The Search for Diabetes in Youth Study, a multicenter, population-based registry of diabetes with diagnosis before 20 years of age, identified 3666 patients with new onset of diabetes in the study areas in 2002–2004. Medical charts were reviewed in 2824 (77%) of the patients in a standard manner to abstract the results of laboratory tests and to ascertain diabetic ketoacidosis at the time of diagnosis. Diabetic ketoacidosis was defined by blood bicarbonate <15 mmol/L and/or venous pH < 7.25 (arterial/capillary pH < 7.30), International Classification of Diseases, Ninth Revision, code 250.1, or listing of diabetic ketoacidosis in the medical chart.

**RESULTS.** More than half (54%) of the patients were hospitalized at diagnosis, including 93% of those with diabetic ketoacidosis and 41% without diabetic ketoacidosis. The prevalence of diabetic ketoacidosis at the diagnosis was 25.5%. The prevalence decreased with age from 37.3% in children aged 0 to 4 years to 14.7% in those aged 15 to 19 years. Diabetic ketoacidosis prevalence was significantly higher in patients with type 1 (29.4%) rather than in those with type 2 diabetes (9.7%). After adjusting for the effects of center, age, gender, race or ethnicity, diabetes type, and family history of diabetes, diabetic ketoacidosis at diagnosis was associated with lower family income, less desirable health insurance coverage, and lower parental education.

**CONCLUSION.** At the time of diagnosis, 1 in 4 youth presents with diabetic ketoacidosis. Those with diabetic ketoacidosis were more likely to be hospitalized. Diabetic ketoacidosis was a presenting feature of <10% of youth with type 2. Young and poor children are disproportionately affected.

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### Key Words

ketoacidosis, adolescent, children, diabetes, type 1 diabetes, type 2 diabetes

### Abbreviations

DKA—diabetic ketoacidosis  
SEARCH—Search for Diabetes in Youth  
IRB—institutional review board  
AIC—Akaike information criterion  
CI—confidence interval  
OR—odds ratio

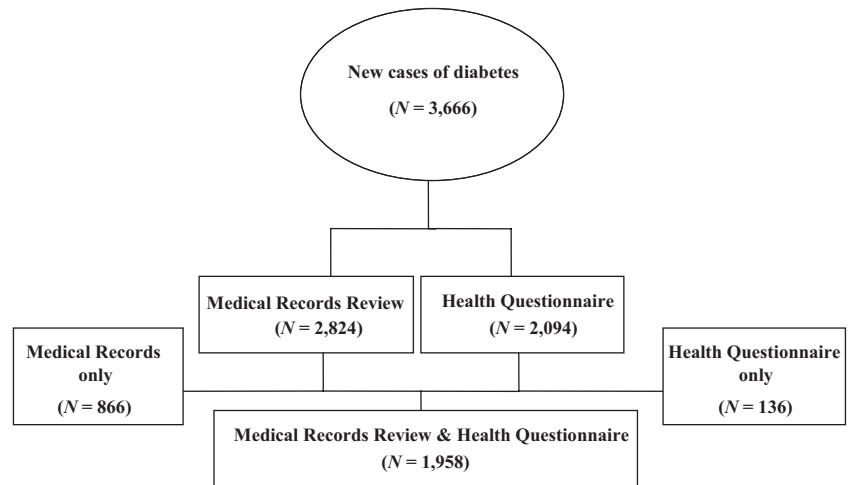
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**I**N THE UNITED States, >150 000 children have diabetes mellitus,<sup>1</sup> and ≥21 000 are diagnosed annually.<sup>2</sup> Over the past 40 years, the incidence of type 1 diabetes in children has been increasing worldwide by 3% to 5% per year.<sup>3,4</sup> In addition, recent reports have suggested that type 2 diabetes in youth has become more common.<sup>5–7</sup> Diabetic ketoacidosis (DKA), the metabolic outcome of very low levels of effective insulin action, can be a life-threatening complication present in 15% to 67% of youth at the time of diagnosis.<sup>8</sup> Despite the high morbidity and cost of DKA at diagnosis of diabetes, there are no recent estimates of its prevalence in the US population. Although predictors of

FIGURE 1  
Number of subjects and sources of data.



DKA in children with established type 1 diabetes have been studied,<sup>9</sup> little is known about predictors of DKA that precede diagnosis. Previous studies have suggested that DKA at the diagnosis of diabetes is more frequent in younger patients, in populations with lower socioeconomic status, and in countries with a lower incidence of type 1 diabetes where diabetes awareness is low.<sup>10-12</sup> Type 2 diabetes may also present with DKA, but the prevalence and predictors of such a severe presentation of type 2 diabetes in youth have not been systematically studied.

To address these issues, the Search for Diabetes in Youth (SEARCH) Study ascertained the prevalence of DKA at diagnosis of diabetes in a large multiracial sample of US youth with diabetes diagnosed before 20 years of age. The spectrum of severity of presentation and the potentially preventable causes of DKA were explored. We hypothesized that lower socioeconomic status and insufficient insurance coverage at the time of diagnosis would both independently increase the risk of DKA. This report also provides preliminary data concerning patterns of the initial delivery of diabetes care to US children and adolescents.

## METHODS

### Human Subjects

Data for this analysis derive from the incidence component of SEARCH. The study protocol was reviewed and approved by the local institutional review board(s) (IRB) that had jurisdiction. Written informed consent for the study visit was obtained according to the local IRB requirements from patients aged  $\geq 18$  years or from a participant's parent or guardian if the age was  $< 18$  years. Written assent was also obtained from patients  $< 18$  years as governed by local IRB instructions. All of the centers complied with the privacy requirements of the Health Insurance Portability and Accountability Act. At some centers, medical charts were reviewed without written consent based on a judgment by the local IRB(s) that the study met the federal requirements for a waiver of consent.

### Overview

A detailed description of the SEARCH methods has been published elsewhere.<sup>13</sup> Briefly, SEARCH is an ongoing 6-center study that, in 2002, began population-based ascertainment of incident cases of diabetes in youth  $< 20$  years of age. Cases are identified as follows: (1) in geographically defined populations in Ohio, Washington, South Carolina, and Colorado; (2) among health plan enrollees in Hawaii (Hawaii Medical Service Association, Med-Quest, and Kaiser Permanente Hawaii) and in southern California (Kaiser Permanente); and (3) coordinated by the Colorado site, among young people listed on rolls of health service beneficiaries in 4 American Indian populations in Arizona and New Mexico. Cases of diabetes are considered valid if diagnosed by a health care provider. Networks of reporting providers are the primary source of identification of incident cases.

Youth with diabetes identified by the SEARCH recruiting network are asked to complete a survey that includes their age at diagnosis, treatment history, and race or ethnicity. Youth who complete the survey are invited to a study visit. Participants in that visit are asked to complete a health questionnaire, which collects information on use of medical care, family income, health insurance, parental education, and family history of diabetes.

This report includes 3666 patients aged  $< 20$  years with new-onset diabetes who were diagnosed in the study areas in 2002–2004. Medical charts were reviewed in 2824 (77%) of these patients; in addition, 2094 (58%) of the participants completed the health questionnaire. The data sources are summarized in Fig 1. Attempts were made for all of the newly diagnosed patients to review their medical charts for the period from diagnosis to a time 6 months after diagnosis. Medical charts were the source of information on the prevalence of DKA at diagnosis and on the use of hospital, emergency, or outpatient services. Availability of medical charts data was related to center and was less complete for patients aged 15 to 19 years and patients with lower family income, Medicaid insurance, and a clinical diagnosis of

type 2 diabetes. Because information about insurance, income, education, and family history was not consistently available in the medical charts, the associations between these factors and DKA at diagnosis were examined only in those patients for whom both medical charts and data from the health questionnaire were available.

### Definition of DKA

Based on the availability and completeness of onset medical charts, 3 indicators of DKA listed below were used to define presence of DKA. For DKA to be present,  $\geq 1$  of the following criteria had to be met in the context of hyperglycemia: (1) blood bicarbonate  $< 15$  mmol/l or pH  $< 7.25$  (venous) or  $< 7.30$  (arterial or capillary); (2) International Classification of Diseases, Ninth Revision, code 250.1 at discharge; and (3) diagnosis of DKA mentioned in the medical charts. Of the 721 patients, 66% met criteria 1, 22% met criteria 2, and 89% met criteria 3.

### Definitions of Variables

Age was categorized in groups as 0 to 4, 5 to 9, 10 to 14, or 15 to 19 years. Data on race and ethnicity were based on self-reports or medical charts. Based on 2000 US census classification, participants were categorized as Hispanic, black, Asian or Pacific Islander, American Indian, non-Hispanic white, and multiple, other, or unknown race. Classification of the type of diabetes was based on the clinical diagnosis made by a health care provider and was collected from the providers at the time of the case report to SEARCH or otherwise from medical charts. The clinical type was categorized as follows: type 1, type 2, or other or unknown diabetes type. Family income and history of diabetes were obtained through the health questionnaire. Responses to questions about health insurance sources, which permitted multiple choices, were categorized hierarchically as private only, private plus anything else, Medicaid only, other, and none. Patients with the Indian Health Service as their only insurance source are included in "other." Parental educational attainment is that of the parent with the higher attainment.

### Statistical Analysis

Statistical analyses of the data were performed using SAS 9.1 (SAS Institute, Cary, NC). Prevalence (percentage) of DKA among incident cases at the time of diagnosis was calculated. Descriptive statistics were calculated for the demographic characteristics. Univariate analyses used the  $\chi^2$  test for ordinal measures. Univariate and multivariate logistic regression analyses were used to identify factors associated with DKA at the time of diagnosis. The Hosmer-Lemeshow method was used to assess goodness of fit. Collinearity was evaluated by inspection of tolerance warnings, SEs, and correlation.

Because the markers of lower socioeconomic status (family income, health insurance, and parental education) were correlated (pairwise Spearman correlation coefficients between 0.3 and 0.5;  $P < .0001$  for all), 3 separate logistic regression models were obtained to ex-

**TABLE 1** Characteristics of Patients With Medical Charts and Prevalence of DKA at Diabetes Diagnosis (N = 2824)

Characteristic	Distribution %	Prevalence of DKA		
		n/N	Prevalence %	<i>P</i> <sup>a</sup>
All		721/2824	25.5	
Age at diagnosis, y				<.001
0–4	16.2	171/458	37.3	
5–9	25.7	194/726	26.7	
10–14	38.8	276/1096	25.2	
15–19	19.2	80/544	14.7	
Gender				.6
Female	50.5	358/1426	25.1	
Male	49.5	363/1398	26.0	
Race/ethnicity <sup>b</sup>				.137
American Indian	2.0	12/56	21.4	
Asian or Pacific Islander	3.7	17/105	16.2	
Black	14.6	100/412	24.3	
Hispanic	14.3	109/404	27.0	
Non-Hispanic white	60.6	441/1712	25.8	
Clinical diabetes type				<.001
1	80.0	664/2260	29.4	
2	18.0	49/507	9.7	
Other/unknown	2.0	8/57	14.0	

<sup>a</sup> Data show the probability that prevalence of DKA was the same (by category).

<sup>b</sup> Race/ethnicity was multiple, other, or missing in 135 subjects (4.8% of the cases).

amine the association of income, insurance, and education with DKA at diagnosis. The Akaike information criterion (AIC) for each model was used to determine the best nonnested model among the measures of socioeconomic status, with the lowest AIC representing the best model fit. All of the tests were 2-sided, and a *P* value of  $< .05$  was considered significant.

### RESULTS

Overall, 54% of the 2824 patients with medical charts available were hospitalized at the time of diagnosis; another 10% were seen only in an emergency department, and 28% were seen at diagnosis on an outpatient basis only. Data were not available for 8% of patients. Among the 721 patients presenting in DKA, 93% were hospitalized, and the remaining were treated in the emergency department only (for 2, specific information was missing). Of those without DKA, fewer were hospitalized (41%;  $P < .001$ ), and an additional 7% received care only in an emergency department. Overall, 44% (668 of 1531) of hospitalizations at diagnosis were because of DKA.

Demographic characteristics, distribution of diabetes type, and the prevalence of DKA by age, gender, race or ethnicity, and diabetes type in the 2824 patients with medical chart data are shown in Table 1. The prevalence of DKA at the time of diagnosis was 25.5% (95% confidence interval [CI]: 23.9%–27.1%). Prevalence decreased significantly with age from 37.3% (95% CI: 32.9%–41.8%) in children aged 0 to 4 years to 14.7% (95% CI: 11.7%–17.7%) in those aged 15 to 19 years. Prevalence did not differ significantly by gender or race/ethnicity. As expected, DKA at diagnosis occurred significantly more often in patients with type 1 diabetes

**TABLE 2** Characteristics of Patients With Data From Both the Medical Chart and Health Questionnaire, Prevalence (%) of DKA at Diabetes Diagnosis, and Unadjusted ORs for DKA

Characteristic	Distribution %	Prevalence of DKA			
		n/N	Prevalence %	OR	95% CI
All	NA	531/1958	27.1	NA	NA
Age at diagnosis, y					
0–4	17.6	131/344	38.1	3.9	2.6–5.8
5–9	28.6	151/560	27.0	2.4	1.6–3.4
10–14	39.2	210/767	27.4	2.4	1.7–3.5
15–19	14.7	39/287	13.6	1.0	Referent
Gender					
Female	50.5	264/988	26.7	1.0	0.8–1.2
Male	49.5	267/970	27.5	1.0	Referent
Race/ethnicity <sup>a</sup>					
American Indian	1.9	8/37	21.6	0.7	0.3–1.6
Asian or Pacific Islander	3.5	12/69	17.4	0.6	0.3–1.1
Black	12.7	70/248	28.2	1.0	0.8–1.4
Hispanic	12.9	65/253	25.7	0.9	0.7–1.3
Non-Hispanic white	65.3	349/1278	27.3	1.0	Referent
Clinical diabetes type					
1	84.6	497/1656	30.0	1.0	Referent
2	14.4	31/283	11.0	0.3	0.2–0.4
Other/unknown	1.0	3/19	15.8	0.4	0.1–1.5
Family history of diabetes <sup>a</sup>					
Yes	59.2	281/1139	24.7	1.0	Referent
No	40.8	245/784	31.3	1.4	1.1–1.7
Household income, in \$					
Not available	9.2	51/180	26.7	1.5	1.0–2.2
<35 000	26.1	162/508	31.9	1.7	1.3–2.4
35 000–49 999	13.5	86/263	32.7	1.8	1.2–2.6
50 000–74 999	19.2	89/373	23.7	1.2	0.8–1.7
75 000–99 999	14.6	70/284	24.7	1.2	0.8–1.8
≥100 000	17.4	72/339	21.2	1.0	Referent
Insurance type <sup>a</sup>					
Private only	67.0	321/1303	24.6	1.0	Referent
Private and something else	7.5	44/145	30.3	1.3	0.9–1.9
Medicaid	19.7	127/384	33.1	1.5	1.2–1.9
Other	3.9	22/76	29.0	1.2	0.7–2.1
None	1.9	13/38	34.2	1.6	0.8–3.1
Parents' highest education <sup>a</sup>					
Less than high school	9.2	55/179	30.7	1.5	1.1–2.2
High school graduate	23.1	135/449	30.1	1.5	1.0–2.2
Some college/AA/trade or technical	34.9	194/679	28.6	1.4	1.0–2.0
College graduate or more	32.6	143/635	22.5	1.0	Referent

AA indicates associate of arts; NA, not applicable.

<sup>a</sup> Race/ethnicity was multiple, other, or missing in 74 subjects (3.8%); family history of diabetes was missing in 35 subjects (1.8%), as were insurance type in 12 (0.6%) and parents' highest education in 16 (0.8%).

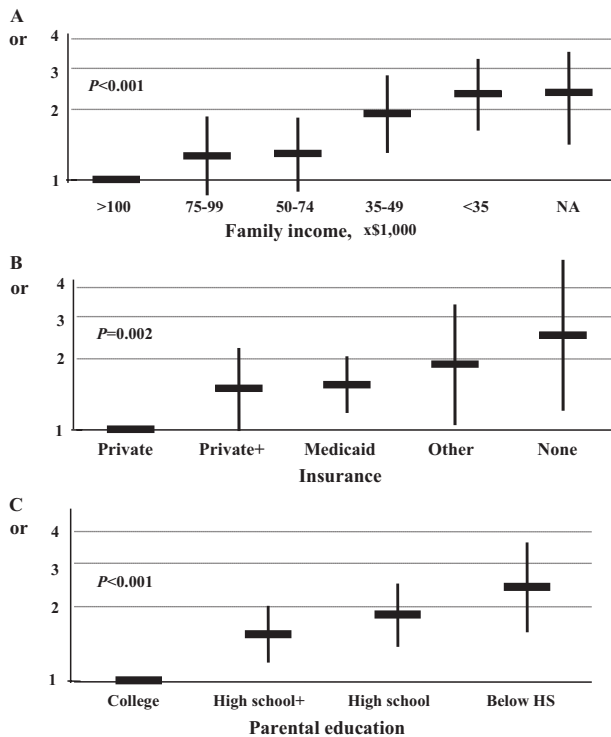
(29.4%; 95% CI: 27.5%–31.3%) than in those with type 2 (9.7%; 95% CI: 7.1%–12.2%).

Of the 507 patients with type 2 diabetes, 26% were hospitalized at diagnosis, 8% were seen only in an emergency department, and 42% were diagnosed in an outpatient setting (data were unavailable for the remaining 24%). All but 17 of these 507 patients were older than 10 years at diagnosis. The prevalence of DKA at diagnosis was 11% and 9% in those aged 10 to 14 and 15 to 19 years, respectively. In these patients, DKA was not significantly associated with gender or race/ethnicity (data not shown).

Demographic and socioeconomic characteristics of the 1958 patients with data from both the medical chart and the questionnaire are summarized in Table 2, along

with the prevalence of DKA at diagnosis in subgroups and unadjusted odds ratios (OR) for DKA. The associations of DKA with age, gender, race or ethnicity, and diabetes type were generally the same for this subset of patients as in the larger group of patients with medical charts available. Patients without a family history of diabetes had a 40% higher OR of presenting with DKA than did those who had a relative with diabetes.

The prevalence of DKA was significantly associated with family income. The OR for DKA was 70% to 80% higher in patients with income below \$50 000 compared with those with family income greater than \$100 000. In all, 75% of the youth had private health insurance; 20% had Medicaid only; and just 1.9% (38 patients) had no medical insurance. Patients with private insurance were



**FIGURE 2**  
Relationship between annual family income (A), insurance type (B), or parental education (C) and the presence of DKA at diagnosis of diabetes in youth. ORs and the 95% CIs were adjusted for center, age, gender, race or ethnicity, type of diabetes, and family history of diabetes.

least likely to present with DKA at diagnosis, whereas the OR was 50% higher in children with Medicaid coverage and 60% higher in those with no insurance. The prevalence of DKA was significantly higher in persons from families with lower parental education (OR: 1.5; 95% CI: 1.1–2.2 for less than high school graduate versus college graduate).

The results of the separate multiple logistic regression models used to examine the associations of the 3 correlated indicators of socioeconomic status with DKA at diagnosis are shown in Fig 2. DKA was significantly associated with each of the indicators, that is, lower family income ( $P < .001$ ; Fig 2A), less favorable health insurance ( $P = .002$ ; Fig 2B), and less parental education ( $P < .001$ ; Fig 2C) after adjustment for center, age, gender, race or ethnicity, diabetes type, and family history of diabetes. The 3 models were almost equivalent (AIC of 2165.5, 2167.1, and 2165.6, respectively), confirming that each of these indicators of socioeconomic status predicts DKA at the diagnosis of diabetes.

Finally, to explore the potential influence of socioeconomic factors on the associations between DKA at diagnosis and age, family history of diabetes, or type of diabetes, a model was fit that included all 3 of the correlated socioeconomic indicators at once (AIC = 2152.9). DKA was strongly associated with younger age, independent of the socioeconomic factors, suggesting that an age-dependent biological factor may be operating as well. Children aged 0 to 4 years were almost 3

times as likely to present in DKA (OR: 2.7; 95% CI: 1.8–4.2) as those aged 15 to 19 years. The risk of DKA was also higher in children aged 5 to 9 and 10 to 14 years old when these groups were compared with the oldest age group (OR: 1.6, 95% CI: 1.1–2.5 and OR: 2.0; 95% CI, 1.4–3.0, respectively). Adjustment for all 3 of the socioeconomic indicators also did not substantially change the associations of DKA at diagnosis that were shown in Table 2 with absence of a family history of diabetes and type of diabetes.

## DISCUSSION

The major finding in this large, population-based study is that a substantial percentage (29.4%) of youth in the United States who are currently being diagnosed with type 1 diabetes present with potentially life-threatening ketoacidosis. This estimate is similar to those reported 10 to 20 years ago from several European countries<sup>10,11,14,15</sup> (Table 3). Although we found that low socioeconomic status, insufficient health insurance, and lower parental education were independently associated with the risk of DKA, we also found that >20% of children from the most affluent families have DKA at diagnosis. This high prevalence of DKA at diagnosis of diabetes among US youth suggests that efforts aiming at preventing this frequent severe complication of diabetes are warranted.

Comparisons with previous studies in the United States and elsewhere suggest that the risk of DKA at diagnosis has not improved decisively over the past 20 years. In Colorado, over the past 23 years, the proportion of children with type 1 diabetes who have presented with DKA at the time of diagnosis has decreased only modestly, from 38% in 1978–1982 to 29% in 1998–2001.<sup>16,17</sup> On the other hand, the incidence of type 1 diabetes in youth is doubling every 2 decades,<sup>3,4</sup> and several studies have reported increasing rates of type 2 diabetes in youth, especially in nonwhite ethnic groups.<sup>5–7</sup> Although the rates of DKA are somewhat lower, with more youth with diabetes, in the absence of community efforts to increase public awareness of the early symptoms of diabetes, DKA is likely to remain a major cause of morbidity and health care expenditures in youth.

Currently, there are few population-based epidemiologic data on the prevalence and predictors of DKA at the time of presentation of type 2 diabetes in youth. In this study, using a large number of patients with type 2 disease from several settings and geographic areas, we found that 9.7% of youth with type 2 diabetes presented with DKA. This finding is consistent with previous reports.<sup>18,19</sup> DKA in adults occurs in those with ketosis-prone diabetes and particularly in nonwhite persons with type 2 diabetes.<sup>20,21</sup> Our finding suggests that DKA at diagnosis should not be used to exclude the diagnosis of type 2 diabetes, at least in patients <20 years of age.

Similar to other population-based studies, we used a clinical definition of diabetes type assigned by health care providers, the only one that could be applied to all of the patients. In >60% of the cases, the initial diagnosis was reported by pediatric or adult endocrinologists. Diabetes type was further characterized in a subset of

**TABLE 3** Prevalence of DKA at Diagnosis of Diabetes in Youth: Literature Review

Country (Source)	Age, y	N	Completeness of Record Review	Study Period	Definition of DKA	Prevalence of DKA, %	Predictors
United States (current study)	0–19	2824	77% population based	2002–2004	pH <7.3 (venous) or pH <7.25 (arterial) bicarbonate <15 or ICD-9 250.1 or Medical chart diagnosis	29 type 1, 10 type 2	Younger age, lower family income, under insurance, lower parental education
United States <sup>24</sup>	0–18	359	94% clinic series	2002–2003	pH <7.3 or bicarbonate ≤15	—	Younger age, lack of insurance
United States <sup>23</sup>	0–18	139	68% hospital series	1995–1998	pH <7.3	38	Younger age, lack of insurance
United States <sup>40</sup>	0–5	247	Hospital series	1990–1999	pH <7.3 or bicarbonate <15	44	
Europe (11 countries) <sup>11</sup>	0–14	1260	91% varied by center	1989–1994	pH <7.3	26–67 (42)	Area of low incidence of type 1 diabetes
Germany <sup>14</sup>	0–14	2121	97% population based	1987–1997	pH <7.3 or bicarbonate <15	26	Lower socioeconomic status
United Kingdom <sup>26</sup>	0–15	328	Hospital series	1987–1996	pH ≤7.25 (arterial) or bicarbonate ≤15	27	Asian minority and age <5 y
United Kingdom <sup>10</sup>	0–20	230	Population based	1985–1986	pH <7.36 or bicarbonate <21	26	Younger age
		97		1990		26	
Ireland <sup>15</sup>	0–14	283	72% population based	1997–1998	pH <7.3	31	

youth participating in the research visit, using clinical and biochemical characteristics, including GAD65 autoantibodies, and the results suggest that the biochemical and clinical characteristics strongly support the clinical assignment of diabetes type.<sup>22</sup> In addition, of 29 subjects with clinical type 2 diabetes who met our criteria for DKA, 17% were GAD56Ab positive, compared with 19% among those who did not meet the criteria for DKA. Moreover, the majority of GAD65-positive participants with type 2 diabetes were overweight and of minority racial or ethnic background, and more than half had GAD65 titers <2 times the cut point used to define positivity, suggesting that most of these participants have type 2 diabetes. Taken together, these data suggest that misclassification of diabetes type is unlikely to have substantially influenced our findings.

This report is in agreement with previous studies regarding the socioeconomic status of patients presenting with DKA. Children in low-income families have higher rates of DKA, and it is frequently more severe.<sup>23</sup> Many children in the United States are either uninsured (9.3 million [12.3%]) or covered by Medicaid only (18.2 million [24%]). In contrast, only 2% of SEARCH participants were uninsured, a low proportion in part because of the settings in which subjects were ascertained. The proportion of Medicaid recipients in SEARCH (19%) was closer to the national average, however. Our data confirm previous reports suggesting that lack of insurance and less favorable health insurance are associated with more severe onset of diabetes in youth.<sup>23–25</sup>

We did not find any significant differences in the prevalence of DKA among different racial and ethnic groups in univariate and multivariate analyses. This is consistent with a previous report on predictors of recurrent DKA in the US youth with type 1 diabetes,<sup>9</sup> where rates were similar in Hispanics and non-Hispanic whites. In contrast, young Asian children in the United Kingdom had 8 times the risk of presenting in DKA as did non-Asian children of the same age.<sup>26</sup>

In agreement with previous studies,<sup>10,11,23,24</sup> we found that the prevalence of DKA was significantly higher among younger children, reaching 37% in those aged 0 to 4 years (Table 1). The strong association with younger age was independent of indicators of socioeconomic status, suggesting a biological, rather than a social, phenomenon. Although DKA is overlooked in some younger children, with presenting symptoms such as vomiting and respiratory distress initially ascribed to less-specific diagnoses,<sup>23</sup> a body of evidence points toward a shorter prodromal period in younger children.<sup>11,27</sup> In developed countries, earlier studies have suggested that as many as 1% of children used to die at the diagnosis of diabetes.<sup>28</sup> The methods of case ascertainment in SEARCH may have missed a small number of case children who died, and we were not able to estimate mortality at diagnosis for the SEARCH population. If the mortality is still as high as 0.31%, that translates into 47 potentially preventable deaths among an estimated 15 000 children and adolescents diagnosed in the United States annually. Complications of DKA, especially brain edema,<sup>29,30</sup> account for nearly all of the deaths at diagnosis of diabetes in this age group.

Our study also shows that, among youth, the use of health care resources at the diagnosis of diabetes is very high, with more than half of the patients being hospitalized and nearly half (44%) of the hospitalizations because of DKA. Many US children are hospitalized for a few days at diagnosis of diabetes, but some of these hospitalizations might be avoided if adequate reimbursement and safe outpatient alternatives for initial care existed.<sup>31</sup> In Colorado, the availability of a tertiary type 1 diabetes outpatient care center has contributed to a decline in hospitalization at diagnosis from 88% in 1978–1982 to 46% in 1998–2001; correspondingly, however, the proportion of hospitalizations because of DKA increased from 44% to 63%.<sup>16,17</sup>

Longitudinal data for trends in the prevalence of onset DKA are scarce. Admission rates for any DKA, at

onset or later in the course of disease, have remained high (>20/100 000 per year) and unchanged in Canadian youth between 1991 and 1999.<sup>32</sup> The US National Diabetes Surveillance System has estimated that the number of hospitalizations for any DKA among persons <45 years of age has increased from 37 000 (24/100 000) in 1980 to 87 000 (47/100 000) in 2003. Although the rates have nearly doubled, the average length of hospital stay in this group has decreased from 6.4 to 3.4 days. ([www.cdc.gov/diabetes/statistics/dkafirst/index.htm](http://www.cdc.gov/diabetes/statistics/dkafirst/index.htm), last accessed December 2006). High rates of hospitalization increase the cost of diabetes care at the time of diagnosis. The annual cost of treating DKA in patients of all ages, at diagnosis and later on, exceeds \$1 billion<sup>33</sup>; newly diagnosed patients account for 25% of this cost.<sup>25</sup>

In light of the increasing incidence of diabetes in the United States and worldwide, a high index of suspicion on the part of parents and health care providers may reduce the cost of initial diabetes care. Early recognition of the classical triad of polydipsia, polyuria, and polyphagia with weight loss (present also in many cases of type 2 diabetes before diagnosis) is essential, as is awareness of the variable presenting symptoms, for example, vomiting or rapid breathing in a young child. An intensive community intervention to raise awareness of the signs and symptoms of childhood diabetes among school teachers and primary care providers in a region of Italy was found to reduce the prevalence of DKA at diagnosis of type 1 disease from 83% to 13%.<sup>34</sup> In the United States, the Diabetes Autoimmunity Study in Youth, an observational study following children at high risk for type 1 diabetes by periodic testing for diabetes autoantibodies, levels of hemoglobin A1c, and random blood glucose, demonstrated that the clinical course of diabetes is milder in youth diagnosed without DKA.<sup>35</sup> Children followed by the Diabetes Autoimmunity Study in the Young were rarely hospitalized and did not develop DKA at diagnosis of diabetes, in contrast to community control subjects with and without a family history of diabetes. They also had nearly normal hemoglobin A1c values at diagnosis, with significantly lower requirements for insulin in the first year of illness. This milder clinical course at diagnosis may have very important long-term implications because near-euglycemic control at onset occurring spontaneously<sup>36</sup> or achieved by intensive insulin treatment<sup>37</sup> has been shown to preserve the secretion of insulin. Residual endogenous insulin secretion, as shown by the Diabetes Control and Complications Trial, predicted a 65% lower risk of severe hypoglycemia<sup>38</sup> and a 50% lower risk of the progression of diabetic retinopathy.<sup>39</sup>

The principal strength of our data is the population-based ascertainment of diabetes cases in a diverse population of US youth, with a resulting large sample size of youth with diabetes. The study includes patients diagnosed in the community setting, overcoming problems in previous research, which has been based exclusively on tertiary care data. The patients in the study included a range of racial or ethnic groups and geographic regions, and the ascertainment process followed a uniform and standard protocol at all of the centers. In addition,

our definition of DKA is likely to capture DKA cases more consistently than earlier reports, where the definition was limited to biochemical data that was not always available in medical charts (especially outpatient records). Finally, our study ascertained all types of diabetes, including type 2, and provided novel observations regarding the presentation of type 2 diabetes in youth.

One of the limitations of this study is that medical charts were not abstracted for 23% of the patients. Health Insurance Portability and Accountability Act privacy laws implemented during the course of the study prevented medical chart abstraction without consent at some SEARCH clinical sites. Patients with abstraction of the medical chart were younger and included a higher proportion of non-Hispanic whites and Hispanics and clinical diagnosis of type 2 diabetes compared with those whose records were not available, potentially leading to some overestimation of the prevalence rates. On the other hand, we may have slightly underestimated rates of DKA because of lower availability of medical charts data at the time of diagnosis for patients with lower family income or Medicaid insurance. Information concerning health insurance, family income, parental education, and family history of diabetes was available only for 53% of all of the patients registered with diabetes ( $n = 3666$ ), and more in-depth analyses of these factors need to be deferred to future studies.

## CONCLUSIONS

In conclusion, at the time of the initial presentation of diabetes in youth in the United States, we estimate that slightly more than one half of patients are hospitalized. In addition, we found that 29.4% of those with type 1 diabetes and 9.7% of those with type 2 were diagnosed with DKA. Young and poor children were disproportionately affected, but DKA occurred even in affluent and well educated families. The prevalence of DKA at the diagnosis of diabetes continues to be high. Increased public awareness and greater medical alertness concerning the symptoms and signs of diabetes are warranted. Improved access to care may additionally reduce the severity and costs of initial diabetes treatment in youth.

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**Presence of Diabetic Ketoacidosis at Diagnosis of Diabetes Mellitus in Youth: The Search for Diabetes in Youth Study**

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