

Reference	Methods	Measures of DKA Association/Risk	Comments
<b>Bohn 2015</b> <sup>29</sup>	Multiple Poisson regression models adjusted for age, sex, and diabetes duration, with treatment center as a random factor provided adjusted estimates of the incidence of DKA events per 100 PY: mean (standard error)	Adjusted estimate of DKA events per 100 PY: mean (standard error) Inactive patients (n=11,357): 6.48 (0.03) Patients who were physically active 1–2 times per week (n=3459): 3.99 (0.03) Patients who were physically active >2 times per week (n=3212): 2.40 (0.03)	<b>A significant inverse association was found between rates of DKA and level of physical activity</b> for the overall study population and for all subgroups (all $P < 0.0001$ )
<b>Bryden 2003</b> <sup>30</sup>	Multiple and logistic regression analyses with dependent variables: psychiatric referral, recurrent DKA admissions over the study period, any serious diabetic complication, HbA1c, and psychiatric symptoms at follow-up Independent variables entered into the model at baseline were sex, psychiatric symptoms, HbA1c, duration of diabetes, BMI, number of daily injections, and marital status Sex and baseline psychiatric symptoms were forced into the model, but other covariates that were not statistically significant at the 10% level were excluded from final models	Presence vs absence of psychiatric symptoms at baseline: <b>OR: 9.1; 95% CI: 2.9 to 28.6; <math>P &lt; 0.0001</math></b> for recurrent admissions for DKA	<b>Patients with recurrent admissions for DKA over the study period were significantly more likely to have developed diabetic complications at follow-up than patients without recurrent DKA admissions</b> , and in multiple regression analyses, recurrent admissions for DKA over the study period predicted psychiatric symptoms at follow-up
<b>Butalia 2013</b> <sup>22</sup>	Logistic regression was used to calculate simple bivariate ORs for the associations between the DKA outcome and individual predictor variables. This was then followed by multivariable logistic regression modelling, for which backward elimination was performed to construct a parsimonious prediction model Variable elimination was carried out in thematic groups: the healthcare system, socioeconomic status, comorbidities, diabetes complications, indicators of complications, BMI, age, and sex	In univariate analyses, DKA hospitalization was associated with: Younger age <b>OR: 0.98 per year; 95% CI: 0.97 to 0.99</b> Lower BMI <b>OR: 0.94; 95% CI: 0.92 to 0.97</b> Shorter duration of T1D <b>OR: 0.97 per year; 95% CI: 0.96 to 0.98</b> Use of statin medications lowered the risk of DKA hospitalization <b>OR: 0.60; 95% CI: 0.42 to 0.86</b> Several comorbidities and complications were associated with increased risk of DKA hospitalization: Gastroparesis <b>OR: 3.85; 95% CI: 1.90 to 7.89</b> Psychiatric diagnosis <b>OR: 1.90; 95% CI: 1.21 to 2.97</b> Increased eGFR <b>OR: 1.12 per 10 mL/min 1.73 m<sup>2</sup>; 95% CI: 1.06 to 1.17</b> Higher HbA1c <b>OR: 1.29 per 1% increase; 95% CI: 1.20 to 1.39</b> was associated with DKA hospitalization Higher quartiles of income compared with the lowest quartile (quartile 2, <b>OR: 0.66; 95% CI: 0.46 to 0.96</b> ; quartile 3, <b>OR: 0.66; 95% CI: 0.45 to 0.95</b> ; quartile 4: <b>OR 0.8; 95% CI: 0.68 to 0.96</b> ) and more formal education ( <b>OR: 0.42; 95% CI: 0.18 to 0.97</b> ) lowered the odds of DKA hospitalization In multivariable logistic regression, longer duration of T1D was associated with lower odds of DKA hospitalization ( <b>OR: 0.96 per year; 95% CI: 0.95 to 0.98</b> ). Other factors significantly associated with DKA hospitalization included gastroparesis ( <b>OR: 4.13; 95% CI: 1.82 to 9.35</b> ), psychiatric diagnosis ( <b>OR: 1.98; 95% CI: 1.22 to 3.19</b> ), and higher HbA1c ( <b>OR: 1.25; 95% CI: 1.16 to 1.35</b> )	

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<b>Butalia 2014</b> <sup>23</sup>	Multivariate logistic regression analyses were used to assess the association between driving distance from patient residence to outpatient diabetes care sites and the DKA outcome  Unadjusted and adjusted models for clinical and sociodemographic factors also were constructed for DKA hospitalization. Clinical factors included BMI, duration of diabetes, specialist care, comorbidities and complications, HbA1c, and eGFR. Other variables included sex, age, median family income, and neighborhood education level (proportion with university degree/diploma/certificate)	In multivariate analyses, driving distance from home to diabetes center 1 (adjusted OR: 1.02 per 1 km; 95% CI: 0.96 to 1.07) to diabetes center 2 (adjusted OR: 1.01; 95% CI: 0.99 to 1.04) or to closest general practitioner (adjusted OR: 0.9; 95% CI: 0.63 to 1.25) was not associated with DKA hospitalization	Patients with DKA hospitalization were younger, had shorter duration of T1D, and had higher HbA1c than patients without DKA hospitalization
<b>Cengiz 2013</b> <sup>24</sup>	Separate logistic regression models were used to evaluate the association between baseline demographic and clinical factors and the occurrence of a DKA event. Factors with a <i>P</i> -value <0.10 from individual factor models adjusted for age were included in an initial multivariate model, and then a backward elimination procedure was used to remove variables with a <i>P</i> -value ≥0.01. Interactions among age, diabetes duration, sex, and HbA1c were evaluated, and no interaction term was significant at the level of 0.01	Detailed data on OR for adjusted and unadjusted models and numerous patient stratifications are available in Table 3 and Supplemental Table 2 of the publication	After adjusting for age, a higher <b>frequency of DKA was significantly associated with female sex, non-white race, lower income, no private insurance, higher HbA1c, and MDI insulin method (vs pump); (all <i>P</i>&lt;0.001).</b>  In a multivariate analysis, <b>female sex, higher HbA1c, non-white race, lower income, and lack of private insurance continued to be significantly associated with a higher frequency of DKA.</b> Results were similar for each age group.
<b>Laimer 2016</b> <sup>42</sup>	Linear regression analysis adjusted for age, sex, duration of diabetes, and basal insulin rate per kg body weight was used to analyze the association between basal rate variability and DKA	In male adult T1D patients, a <b>higher variability index of basal insulin rates was associated with higher frequency of DKA (<i>r</i>=0.04; <i>P</i>=0.029)</b>  Logistic regression analysis (adjusted for age, sex, duration of disease, and total basal insulin) <b>confirmed significant positive correlations of the variability index of basal insulin rates with DKA (<math>\beta</math>=0.012; <i>P</i>=0.017) and between basal insulin rates (basal rate/kg/24h) and DKA (<math>\beta</math>=1.743; <i>P</i>&lt;0.001),</b> but not with age ( $\beta$ =0.008; <i>P</i> =0.159), duration of disease ( $\beta$ =0.001, <i>P</i> =0.884), or sex ( $\beta$ =0.205, <i>P</i> =0.154) and DKA	
<b>Lebenthal 2012</b> <sup>25</sup>	Multiple logistic regression by stepwise backward methods was applied to determine variables significantly associated with acute complications	Overall rates of DKA events were significantly higher in familial than in sporadic cases (2.8 vs 1.9 events per 100 PY) <b>IRR=1.5; 95% CI: 1.03 to 2.22; <i>P</i>=0.03</b>  Note that this association was not significant for patients aged >19 years (IRR=0.92 [95% CI: 0.36 to 2.32], <i>P</i> =0.87)	A higher mean HbA1c level was a predictor for DKA events in both the familial and the sporadic groups, whereas age at diagnosis of T1D and sex did not predict DKA events in either group
<b>Li 2014</b> <sup>44</sup>	A Poisson regression model was used to determine risk factors for secondary DKA. Separate backwards stepwise logistic regression analyses were used to identify risk factors for the recurrence of secondary DKA	Detailed data on relative risk are available in Figure 1 of the publication and results of logistic regression analyses for secondary DKA recurrence are reported in Table 2  For the overall population, the following parameters were significant risk factors for secondary DKA:	There were no significant differences in DKA incidence between patients treated with insulin glargine and patients treated with NPH insulin  Regarding recurrences, 34.4% of secondary DKA episodes represented

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		<p>Female sex (<b>RR=2.12; 95% CI: 1.50 to 3.04</b>)</p> <p>Medical reimbursement rates &lt;50% (<b>RR=1.84; 95% CI: 1.33 to 2.60</b>)</p> <p>Uncontrolled diet ("never controlled" vs "usually controlled") (<b>RR=1.76; 95% CI: 1.18 to 2.57</b>)</p> <p>Smoking (<b>RR=2.18; 95% CI: 1.30 to 3.59</b>)</p> <p>Poor glycemic control (HbA1c per1.0% increase, <b>RR=1.15; 95% CI: 1.10 to 1.21</b>)</p> <p>An overweight/obese BMI (vs normal) significantly reduced the risk of secondary DKA (<b>RR=0.57; 95% CI: 0.31 to 0.96</b>)</p> <p>In logistic regression models, recurrence of secondary DKA was associated significantly with:</p> <p>Female sex (<b>RR=10.56; 95% CI: 1.97 to 56.72; P=0.01</b>)</p> <p>Smoking (<b>RR=6.99; 95% CI: 1.02 to 48.00; P=0.05</b>)</p> <p>Poor <math>\beta</math> cell function (stimulated C-peptide/100 pmol/L decrease (<b>RR=4.22; 95% CI: 1.20 to 6.97; P=0.01</b>))</p> <p>Poor glycemic control (HbA1c per1.0% increase, (<b>RR=1.16; 95% CI: 1.00 to 1.34; P=0.05</b>))</p>	recurrent events ( $\geq 2$ episodes) in 3.8% of the patients
<b>Miller 2015</b> <sup>38</sup>	No statistical modelling analyses reported; qualitative summary data only	NR	The frequency of DKA tended to be higher among participants with higher HbA1c levels and slightly lower among participants using an insulin pump
<b>Shalitin 2012</b> <sup>45</sup>	No statistical modelling analyses reported; summary data only based on Pearson's chi-square test or Fisher's exact test	NR	The rates of DKA episodes were not significantly different between the 2 groups (patients who initiated CSII within 1 year of diagnosis or patients who initiated CSII at least 1 year after diagnosis), either in total or on subanalysis by age groups, pubertal stages, diabetes duration, or CSII treatment duration
<b>Trief 2014</b> <sup>31</sup>	Diabetes-management outcomes (including DKA) in those with and without depression were compared using linear regression for continuous variables and logistic regression models for categorical variables	<p>Compared with non-depressed participants, depressed participants had more frequent DKA events in the past 3 months (<b>11% vs 4%; P&lt;0.001</b> for all 3 definitions of depression)</p> <p>Compared with lower-scoring participants, participants with higher depression scores were more likely to experience more frequent DKA (<b>P&lt;0.001</b>)</p> <p>NR</p>	

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<b>Weinstock 2013</b> <sup>13</sup>	Separate logistic regression models were used to evaluate the association between baseline demographic and clinical factors and the occurrence of a DKA event. Factors with a <i>P</i> -value <0.10 from individual factor models adjusted for age were included in an initial multivariate model, and then a backward elimination procedure was used to remove variables with a <i>P</i> -value ≥0.01	Detailed data on OR and 95% CI from logistic regression models evaluating the association between baseline demographic and clinical characteristics and the occurrence of a patient-reported or clinic-reported DKA event are described for numerous patient subgroup stratifications in Table 2 and Supplemental Table 3 of the publication	Frequency of DKA was lower with increasing age. However, the age effect was largely explained by HbA1c level, which was strongly associated with the occurrence of a DKA event. Frequency of DKA was not associated with diabetes duration  In addition to HbA1c level, <b>a higher frequency of DKA was associated with lower socioeconomic status based on education level, income, and insurance status (<i>P</i>&lt;0.001 for each in multivariate model) and female sex (<i>P</i>=0.008)</b> . In univariate models, non-Hispanic black and Hispanic participants had higher frequencies of DKA than non-Hispanic whites, and current smokers had higher frequency of DKA than nonsmokers, but after adjusting for socioeconomic status, neither factor was significant in the multivariate model. Frequency of DKA was not significantly different between pump and injection users
<b>Wong 2014</b> <sup>20</sup>	Logistic regression modelling adjusted for sex, race/ethnicity, education level, annual household income, health insurance status, diabetes duration, and insulin delivery method (pump/injection)	CGM UYser vs CGM non-user: <u>18 to &lt;26 yrs:</u> Unadjusted OR: 0.5; 95% CI: 0.2 to 1.0; <i>P</i> =0.06 Adjusted OR: 0.6; 95% CI: 0.2 to 1.8; <i>P</i> =0.33 <u>≥26 yrs:</u> Unadjusted OR: 0.7; 95% CI: 0.4 to 1.1; <i>P</i> =0.09 Adjusted OR: 1.4; 95% CI: 0.8 to 2.3; <i>P</i> =0.23	CGM use was not significantly associated with rates of DKA for these age groups in logistic regression models

Key: BMI = body mass index; CGM = continuous glucose monitoring; CI = confidence interval; CSII = continuous subcutaneous insulin infusion; DKA = diabetic ketoacidosis; eGFR = estimated glomerular filtration rate; HbA1c = glycosylated hemoglobin A1c; IRR = incidence rate ratio; NPH = neutral protamine Hagedorn; NR = not reported; OR = odds ratio; PY = person-years; RR = relative risk; T1D = type 1 diabetes mellitus.

Bold text highlights associations that were found to be statistically significant in each study.

\* Associations were calculated based on the full patient population (which included pediatric patients); however, analyses were adjusted for age.