



Burden of Diabetic Ketoacidosis Among People Living with Type 2 Diabetes: A Systematic Review

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Declaration

- Study funded by Abbott Diabetes Care
- CW has received research funding from Abbott Diabetes Care, AbbVie, Bayer, Eli Lilly, and Company, and Novo Nordisk, and has served as a speaker/advisor for Abbott Diabetes Care, Biomea, Eli Lilly and Company, MannKind, Novo Nordisk
- YP and AB are employees of Abbott Diabetes Care

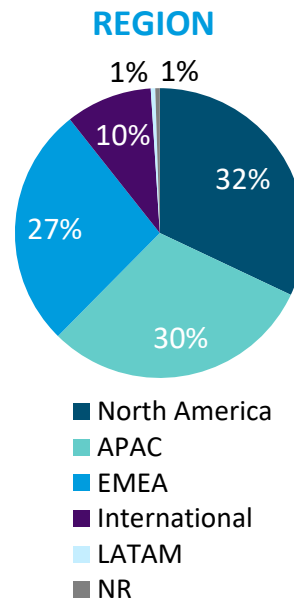
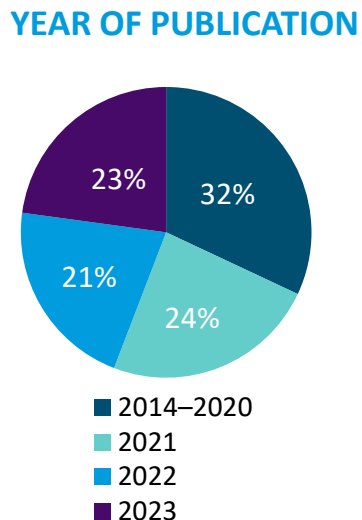
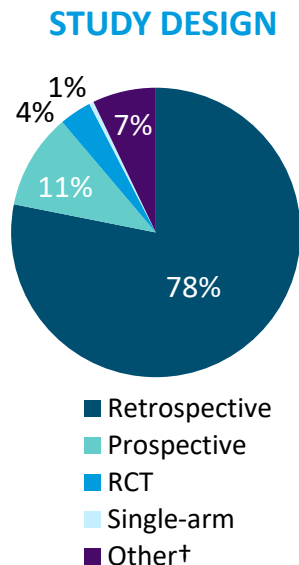
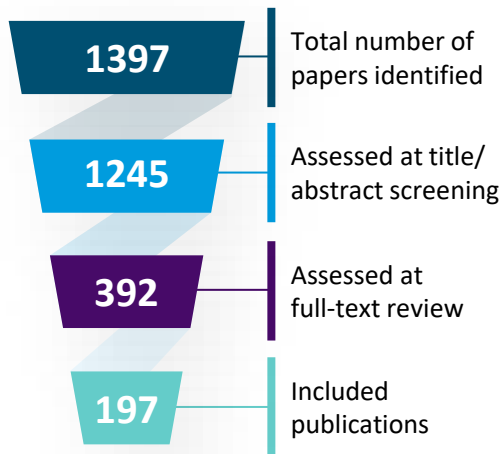
Aim: to assess the burden of diabetic ketoacidosis (DKA) among people living with type 2 diabetes (T2D)

BACKGROUND	<ul style="list-style-type: none"> DKA can be a life-threatening complication that requires timely care¹; frequency of DKA has increased over the years² People living with T1D are known to be susceptible to DKA³ DKA can occur among people with T2D; however, the burden of DKA in T2D is not well defined 			
DATABASES SEARCHED	<ul style="list-style-type: none"> EMBASE MEDLINE Cochrane Library 			
PICOs	<p>PATIENTS People living with T2D</p>	<p>INTERVENTION Any Note: Systematic assessment carried out for people on SGLT2i and / or insulin subgroups</p>	<p>COMPARATOR Any</p>	<p>OUTCOMES Epidemiology, Burden (Clinical, economic, humanistic), risk factors, precipitating factors</p>
STUDY INCLUSION CRITERIA	<ul style="list-style-type: none"> Full-text publications from 2014 to December 2023 Abstracts from 2021-2023 		<ul style="list-style-type: none"> English language Primary literature – interventional or observational studies 	

DKA, diabetic ketoacidosis; SGLT2i, sodium glucose cotransporter 2 inhibitor; T2D, type 2 diabetes

1. Lizzo et al. StatPearls. 2023. Accessed from <https://www.ncbi.nlm.nih.gov/books/NBK560723/> 2. Desai et al. Diabetes Care. 2018. <https://doi.org/10.2337/dc17-1379>
 3. Virdi et al. DTT. 2023. <https://doi.org/10.1089/dia.2023.0149>

Results: Significant variation was observed among studies evaluating burden of DKA



†Others include pooled RCTs, publications with both retrospective and prospective elements, and unclear observational designs

APAC, Asia-Pacific; DKA, diabetic ketoacidosis; EMEA, Europe, Middle-East and Africa; LATAM, Latin America; NR, not reported; RCT, randomized controlled trial

Results: Incidence of DKA was variable

GROUP	RANGE	5 TH - 95 TH PERCENTILE
Across Included Studies	0.0 – 63 per 1000 PY	0.004 – 7.6 per 1000 PY
SGLT2i subgroup	0.0 – 24.5 per 1000 PY	0.2 – 7.6 per 1000 PY
Insulin subgroup	0.5 – 4.9 per 1000 PY	NR

BY COUNTRY	RANGE
USA	0.55 – 9.1 per 1000 PY
OUS	0.001 – 63 per 1000 PY

OTHER SUBGROUPS (NOT SYSTEMATICALLY EVALUATED)	RANGE
Elderly	0.5 – 2.8 per 1000 PY
CKD	2.5 – 4.9 per 1000 PY

CKD, chronic kidney disease; DKA, diabetic ketoacidosis; NR, not reported; OUS, outside US; PY, person-years; SGLT2i, sodium glucose cotransporter-2 inhibitors

Results: Risk Factors and Precipitating Factors of DKA in T2D



RISK FACTORS

- Poor Glycemic Control
- SGLT2i use
- Insulin use

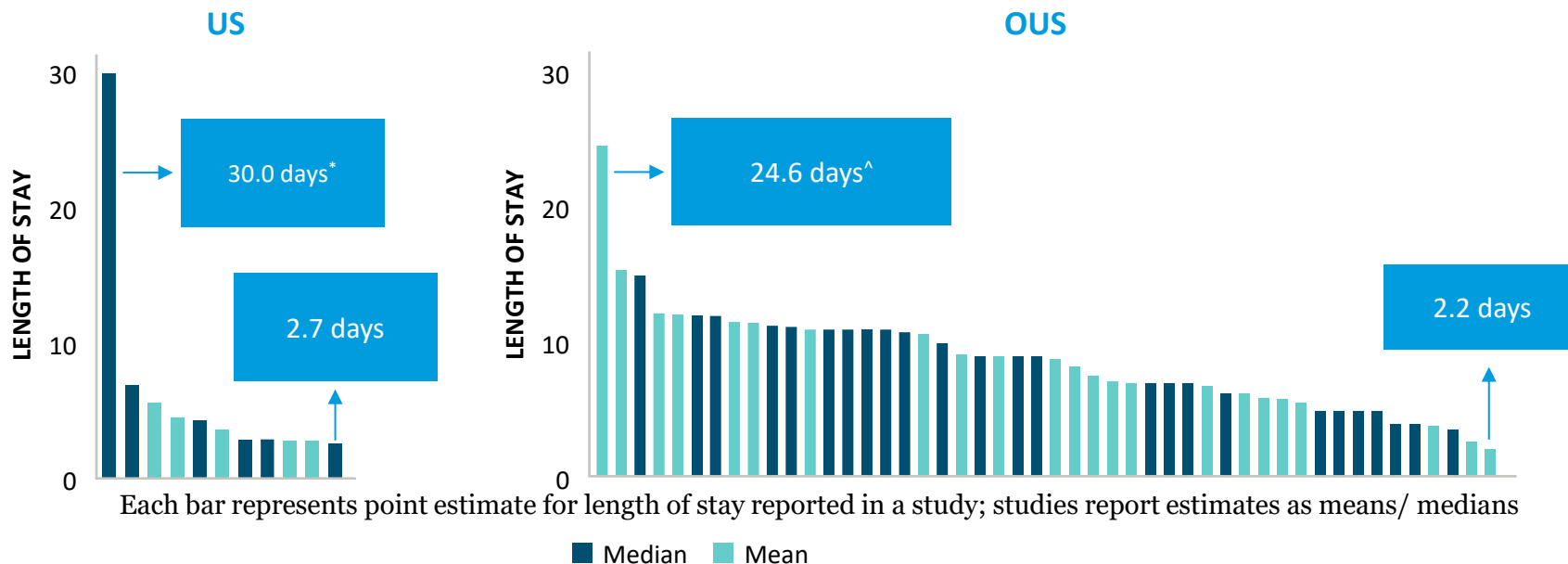


PRECIPITATING FACTORS

- Infection
- Nonadherence to Insulin

DKA, diabetic ketoacidosis; SGLT2i, sodium glucose cotransporter-2 inhibitors; T2D, type 2 diabetes

Results: Length of stay associated with DKA event was variable



*Among patients with COVID-19; ^Among non-SGLT2i users who developed post-operative DKA

Conclusion

THIS SYSTEMATIC REVIEW HIGHLIGHTS THE INCIDENCE OF DKA AMONG PEOPLE WITH T2D

- Groups at higher risk include - people with T2D with poor glycemic control, SGLT2i users, and insulin users

EVIDENTIARY GAPS / AREAS OF FUTURE RESEARCH

- The economic and humanistic burden of DKA among people with T2D
- The impact of potential factors associated with DKA in clinical practice: accuracy of diagnosis of type of diabetes, duration of diabetes, socioeconomic factors, race/ethnicity, alcohol use or nutritional status

LIMITATIONS

- Potential bias based on heterogeneity in study designs, populations, quality of studies, and exclusion of studies not published in English
- Unlikely to capture incidence of mild / euDKA that occurs in routine clinical practice which is frequently missed
- Unlikely to capture incidence of DKA vs. HHS with ketosis that may be difficult to distinguish

Given the burden of DKA in T2D, resources that monitor ketones for patients at high-risk of DKA may reduce the burden on patients and the healthcare system

DKA, diabetic ketoacidosis; euDKA, euglycemic diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state; T2D, type 2 diabetes

Background

- Diabetic ketoacidosis (DKA) can be a life-threatening complication¹
- Frequency of DKA has increased over the years²
- People living with type 1 diabetes (T1D) are known to be susceptible to DKA³
- DKA can occur among people with type 2 diabetes (T2D)
- However, the burden of DKA among people living with T2D is not well understood
- Additionally, data on risks and characteristics of individuals at highest risk of DKA in T2D are unknown

Aims

- Quantify the epidemiological, clinical, humanistic, and economic burden of DKA among people living with T2D

Methods

- Databases searched:** EMBASE, MEDLINE, Cochrane Library (Jan 2014 – Dec 2023)
- Abstracts from ADA, EASD, ATTD** were included for the years 2021 – 2023
- Studies published in English, and primary (interventional or observational) were included in the review
- Pre-specified sub-groups of interest** were patients using sodium glucose co-transporter 2 inhibitors (SGLT2i) and insulin users
- Outcomes of interest included** – epidemiological outcomes (incidence, prevalence, risk factors, predisposing factors), clinical burden, economic burden, and humanistic burden

References

1. Lizzo et al. *StatPearls*. 2023. Accessed from <https://www.ncbi.nlm.nih.gov/books/NBK560723/>
2. Desai et al. *Diabetes Care*. 2018. <https://doi.org/10.2337/18.12.3379>
3. Viridi et al. *DTT*. 2023. <https://doi.org/10.1089/dia.2023.0149>

Conflicts of Interest

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Results

Figure 1: Study Flow

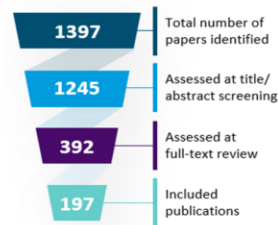
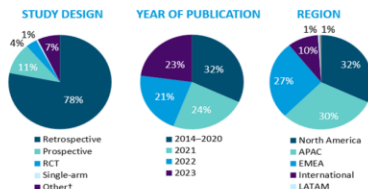


Figure 2: Study Characteristics



*Others include pooled RCTs, publications with both retrospective and prospective elements, and unclear observational designs
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Table 1: Incidence of DKA was Variable

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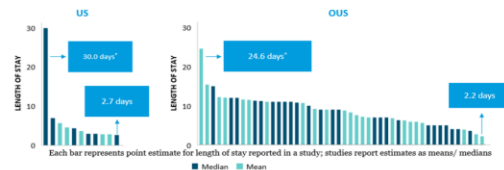
*Not systematically evaluated
 CKD, chronic kidney disease; OUS, outside USA; PY, person years; USA, United States of America

Results (continued)

Table 2: Risk Factors and Predisposing Factors of DKA

Risk Factors	Predisposing Factors
Poor Glycemic Control	Infection
SGLT2i use	Non-Adherence to Insulin
Insulin use	

Figure 3: Length of Stay for DKA related hospitalizations



*Among patients with COVID-19; *Among non-SGLT2i users who developed post-operative DKA

Discussion

- DKA can occur frequently among people living with T2D; risk factors include poor glycemic control, and use of SGLT2i and/or insulin
- DKA can be burdensome for healthcare system with hospitalizations
- Evidentiary gaps associated with economic and humanistic burden of DKA in T2D exist

Given the burden of DKA in T2D, resources that monitor ketones for patients at high-risk of DKA may reduce the burden on patients and the healthcare system