The Economic Impact of Diabetic Ketoacidosis (DKA) in People with T1DM at High Risk for DKA: a Structured Literature Review

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PURPOSE

- Diabetic ketoacidosis (DKA) is a serious complication of diabetes, more common in type 1 diabetes mellitus (T1DM) but also occurs in type 2 diabetes mellitus (T2DM).[1,2]
- DKA is characterised by a triad of hyperglycaemia (or a history of diabetes), ketosis, and metabolic acidosis, with rapid symptom onset.[2] Symptoms include increased thirst, excessive urine production, weight loss, excessive tiredness, nausea, vomiting, dehydration, abdominal pain, hyperventilation, and reduced consciousness.[1-3]
- If unmanaged, DKA requires emergency medical treatment and is life-threatening.[3]
- DKA is particularly prevalent in paediatrics and adolescents with T1DM and in insulin pump-users, resulting in increased hospitalizations, subsequent length of stay (LOS), recurrence, and mortality.[4] For example, DKA per 1,000 in paediatric and adolescent people with Type 1 diabetes mellitus (PwD[T1]) was reportedly higher compared to the overall T1DM population, (108 DKA events per 1,000 patients versus 55.5 per 1,000 patients respectively).[5] With regards to PwD(T1) requiring insulin pump treatment, DKA percentage prevalence prior to pump-usage has been reported to range from 8%–59%.[6,7]
- As the economic burden of DKA is poorly understood, this structured literature review investigated the published economic burden of DKA, with a focus on paediatric and adolescent T1DM, and PwD(T1) treated with an insulin pump or SGLT2 inhibitors (SGLT2i).

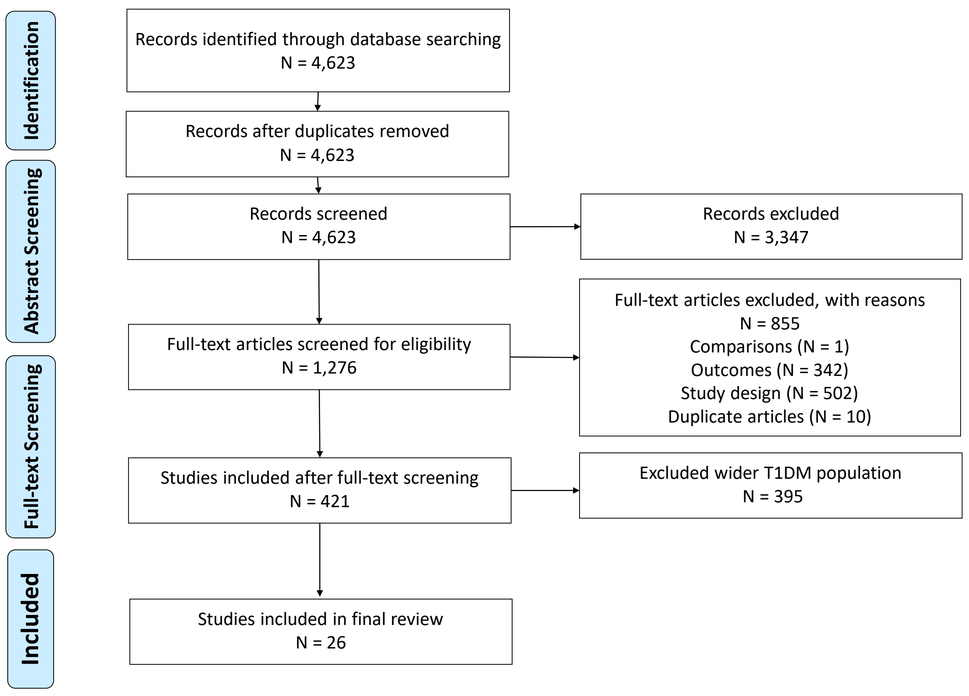
METHODS

- A literature search was conducted using the Ovid platform to search MEDLINE and Embase, using terms for economic burden associated with DKA in T1DM.
- Publication dates were limited from 2011–2021, plus conference proceedings search from 2020 and 2021.
- The identified records were screened by a single reviewer using a pre-specified PICOS criteria for the economic burden of DKA In T1DM .
- A second reviewer performed a quality check of selected records. Any disagreements were resolved via a consensus between the reviewers.
- This record selection process was carried out across title and abstract, and full text screening stages.

RESULTS

- 26 articles discussing the economic burden of DKA in paediatric and adolescent PwD(T1) and insulin pump users were identified.[8-33]
- Included articles were from a wide variety of countries including the US, Australia, UK and other European countries. Study designs included observational, cohort and database studies.
- The findings presented from this review were exploratory in nature due to the highly variable evidence base which differed greatly in terms of study design, sample size and geography. The majority of studies (n =18) also did not report how DKA was defined. The results should therefore be interpreted with caution.

Figure 1. PRISMA Diagram



Economic burden of DKA in paediatric and adolescent PwD(T1)

- Overall, the studies identified highlighted the significant economic burden of DKA in paediatric PwD(T1) and that the average cost of treatment increased from 2006 to 2016.
- 13 studies reported on LOS in hospitals due to DKA in paediatric and adolescent patients.[8-20] The average LOS due to a DKA episode ranged 1–14 days in paediatric patients, with a failure to correct acidosis within 24 hours reportedly increasing the average LOS.[11-13] Severe DKA typically increased hospital LOS by 2 days (see figure 2).[13,20]
- With regards to DKA treatment, eight studies investigated costs, with the cost data reported highly varied between regions.[8,14,18,19,21-24]
- The average cost per DKA episode in paediatric PwD(T1) in 2019 was reported to be £1,387, according to a study conducted in 71 individuals in the UK.[16]
- The average annual cost per patient for paediatric hospital admissions increased from $14,458 to $20,997 between 2006 and 2016; according to a US study taking data from 149,535 patients across 46 states (see figure 3).[8]

Figure 2. Hospital LOS of patients with and without DKA at T1DM onset[13]

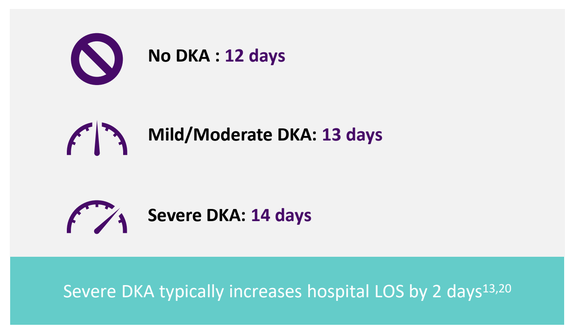
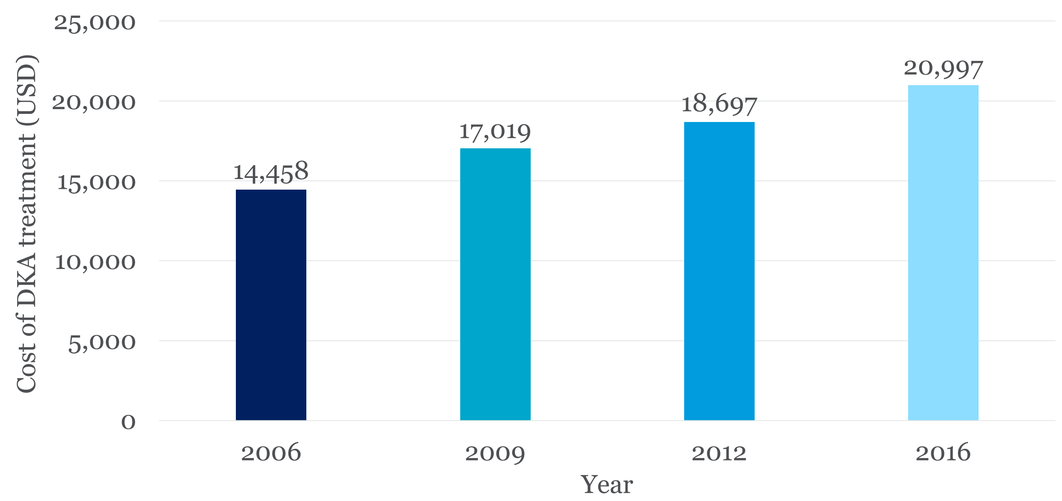


Figure 3. Average cost of DKA hospital treatment for paediatric admissions on a per patient per year basis[8]



Economic burden of DKA in insulin pump-users

- The review identified nine studies reporting on the economic burden of DKA in insulin pump-users, of which eight reported resource-use (hospitalizations and LOS) and one reported cost of treatment.[25-33]
- Although studies were heterogenous, results across studies suggest that hospitalizations due to DKA were prevalent among both pump users and non-pump users with T1DM.[31,32] For example in one study (n=345) the rate of DKA hospitalizations was 2.3 per 100 PwD(T1) in pump users and 4.7 in non-pump users.[32]

SUMMARY – CONCLUSIONS

- Evidence from 26 studies, from multiple countries, consistently demonstrated substantial costs reported for hospitalizations, hospital LOS and patient treatment associated with DKA.
- As the studies identified were from multiple countries with different healthcare systems the reported costs varied greatly. However, the treatment costs of DKA episodes were found to have increased over the years. Therefore, this may indicate that the economic burden of DKA will continue to grow over time, especially since the prevalence of T1DM is increasing in many countries.[33]
- The results suggest that hospitalization due to DKA is prevalent among both insulin pump-users and non-pump users , the hospitalization data demonstrate that pumps are not infallible. Therefore, PwD(T1) being treated with pumps should still monitor their ketone levels as they are still at risk of DKA episodes, and that DKA-related resource use is still required for pump-users.
- There were no data from studies reporting on the economic burden of DKA in PwD(T1) using SGLT2i. This illustrates a clear need for research into the economic consequences of DKA episodes in this population.
- In conclusion, DKA requires extensive resource use in paediatric and adolescent PwD(T1) and insulin-pump-users, leading to substantial economic burden. Increased awareness of DKA and its management should be prioritized to reduce this economic burden.

DECLARATION OF INTEREST

- Biju Varughese was an employee of Abbott Diabetes Care during the time this research was conducted.
- Patrick Lavelle, Rikal Bhaila and Ben Rousseau are employees of Adelphi Values PROVE.
- Adelphi Values PROVE conducted the research, with funding from Abbott Diabetes Care.

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