Continuous ketone monitoring for people with diabetes: international expert recommendations on the application of a new technology

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The ability to reduce the risk of developing diabetic ketoacidosis (DKA) remains a major care gap for people with diabetes, particularly those on intensive insulin therapy. The anticipated availability of continuous ketone monitoring (CKM) has the potential to reduce the risk of developing DKA, one of the most life-threatening acute complications of type 1 and type 2 diabetes. International clinical guidelines have established ketone thresholds for suspected and confirmed diagnoses of DKA, based on use of point-of-care testing, as part of a triad of markers with allied thresholds for hyperglycaemia and acidosis. The increasing occurrence of euglycemic DKA, with glucose concentrations below established diagnostic thresholds, makes the availability and use of CKM technology an important addition to the diabetes management toolkit. CKM data could alert the user when the risk of acute DKA is high on sick days in addition to signalling that individuals might be predicted to be at greater overall risk of future DKA on the basis of the distribution and degree of ketone measures in daily life. If widespread use of CKM devices is to be safe and effective in reducing the occurrence of DKA, it is important to establish clear ketone thresholds which notify CKM users when action on their part is required. In defining these thresholds and actions, it was important to ensure that the CKM user is not exposed to avoidable anxiety or suffers alarm fatigue, thus adding to the burden of living with diabetes. In the absence of substantial evidence that can identify appropriate ketone thresholds for CKM use, a panel of international experts in the management of DKA was convened with the aim of developing a number of objective, practical recommendations on how this novel diabetes technology could improve outcomes for individuals at risk of DKA, the results of which we report in this Personal View. These recommendations have been endorsed by the International Society for Pediatric and Adolescent Diabetes (ISPAD).

Introduction

Diabetic ketoacidosis (DKA) is an acute complication associated mainly with type 1 diabetes, but can occur in type 2 and other forms of diabetes,[1,2] and is one of the most preventable causes of morbidity and mortality for individuals with diabetes.[3] Episodes of DKA are characterised by a triad of hyperglycaemia, hyperketonaemia, and metabolic acidosis. The current diagnostic criteria for DKA in children, adolescents, and adults with diabetes are shown in table 1.[1,2] These guidelines set an objective threshold for β-hydroxybutyrate of 3 mmol/L or higher in cases of suspected DKA. To date, ketone concentrations are not always measured as part of DKA diagnosis, and markers of metabolic acidosis have been emphasised, including serum bicarbonate, anion gap, and venous pH.[4] However, diagnosis of DKA relies on confirmation of diabetes or the presence of hyperglycaemia for the D, ketosis for the K, and acidosis for the A. As part of these diagnostic criteria, a serum β-hydroxybutyrate sample is preferable. The underlying pathophysiology of DKA is expertly reviewed elsewhere[3,5] and is not discussed in this Personal View.

Registry data show that annual rates of hospitalisation for DKA among children and adolescents with type 1 diabetes range from 5·0% to 7·1% across the UK, USA, Germany, and Austria.[6] Emergency room visits and hospital admissions suggest an annual rate of 28 cases per 1000 adults with diabetes in the USA,[7] with increased rates from 2009 to 2015. In Denmark, incidence of DKA in adults doubled between 1996 and 2008, although trends from 2008 to 2020 have seen a modest decrease.[8] Registry data also report annual DKA rates of 1·9–2·8% in adults with type 1 diabetes and 0·5–0·9% for insulin-treated type 2 diabetes in Germany, Austria, and Belgium.[9,10] Data from France indicate annual rates of DKA requiring hospitalisation of 5·5% for adults with type 1 diabetes and 1·7% for adults with type 2 diabetes.[11] It is important to note that admissions for DKA are much more common than for severe hypoglycaemia in children and adults with type 1 diabetes.[11,12]

Longitudinal data indicate that having a DKA episode is associated with significantly increased long-term risks for major adverse cardiovascular events, advanced kidney disease, neuropathy, reduced cognitive function, recurrent DKA, and all-cause mortality.[13,14] For adults with type 2 diabetes, DKA is associated with increased risks for diabetic retinopathy, acute kidney injury, renal failure, and a history of, or recurrent, DKA.[15,16]

Current methods of ketone measurements, capillary blood ketone monitors and urine ketone strips, for use by people at risk of DKA each have advantages and disadvantages (appendix p 2). However, although ketone self-testing is recommended for people with diabetes at times of heightened DKA risk,[17] surveys indicate that few

individuals use them and do not know how to respond to elevated ketones or whether to seek emergency medical care.[18–20] Despite this poor engagement with ketone monitoring, at least one survey has shown that health-care professionals overestimate the knowledge that people with diabetes have regarding DKA.[19] Health-care professionals themselves can also lack important knowledge regarding the symptoms and precipitating factors for DKA, as evidenced by the significant reductions in DKA episodes associated with awareness campaigns targeted at health-care professionals.[21,22] Given the underestimated awareness and effect of DKA for people with diabetes and health-care professionals, the broad implementation of continuous ketone monitoring (CKM) technology has the potential to transform diabetes management for considerable numbers of people at risk of DKA by providing users with immediate feedback on rising ketone concentrations and alerting them when immediate action could be needed. This unmet need is illustrated in the real-life case study in figure 1.

The introduction of CKM devices would also have substantial implications for clinical practice in diabetes. Given that consumers already have access to CKM devices that do not have US Food and Drug Administration or European Medicines Agency regulatory approval, it is important to establish practical recommendations on the alert thresholds and associated actions for CKM users, health-care professionals, and manufacturers and regulators. Other CKM sensors are currently under regulatory review for use as medical technologies and are supported by performance data[23] that show good accuracy for ketone detection.[24] To date, clinical reviews have discussed the potential value of CKM technology,[25] but there has been little discussion of issues associated with the real-world application of CKM devices in diabetes care, particularly how existing guidelines for DKA management[1,2] should be interpreted for CKM users.

In the absence of randomised controlled trials (RCTs) or real-world studies on CKM use, a group of clinical experts in management of DKA in diabetes was convened for a workshop on March 18, 2025, in Amsterdam to establish recommendations for the use of novel CKM technologies in the care of people with diabetes (panel). The participants—a consensus group who also comprise the authors of this Personal View—were drawn from academic and clinical institutions, and from professional medical associations, globally. People living with diabetes were also included from prominent advocacy groups as part of the consensus group. The consensus process followed a Nominal Group Technique methodology, combining brainstorming, discussion, and refinement of ideas, to reach consensus. Only at the final in-person meeting was anonymity not available to the consensus group. Recommendations were agreed by the consensus group as part of manuscript drafting, and following evidence grading according to the American Diabetes Association Standards of Medical Care in Diabetes (panel).

Glycaemia in DKA and euglycaemic DKA

DKA is prevalent in at least 35% of hospital admissions for new-onset type 1 diabetes and is common at presentation for individuals with ketosis-prone type 2 diabetes.[27,28] The prevalence is reflected in the incorporation of glycaemic criteria for diagnosis of DKA within international guidelines (table 1). Better awareness and management of hyperglycaemia using continuous glucose monitoring (CGM) devices is associated with reduced hospital admissions for DKA, in type 1 diabetes and type 2 diabetes.[11,29] However, in the observational studies that have been used to underpin diagnostic criteria for DKA, glucose concentrations are not correlated with bicarbonate concentrations and only weakly correlated with β-hydroxybutyrate concentrations.[30]

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	International Society for Pediatric and Adolescent Diabetes (2022)[2]	International consensus report* (2024)[1]
Hyperglycaemia	>11 mmol/L (>200 mg/dL)	≥11·1 mmol/L (≥200 mg/dL)
Venous pH	<7·30	<7·30
β-hydroxybutyrate	≥3 mmol/L	≥3 mmol/L
Serum bicarbonate	<18 mmol/L	<18 mmol/L

*Endorsed by the American Diabetes Association, European Association for the Study of Diabetes, American Association of Clinical Endocrinology, Joint British Diabetes Societies for Inpatient Care, and Diabetes Technology Society.

Table 1: **Recent International Society Guidelines of markers for diagnosis of mild diabetic ketoacidosis in children and adults**

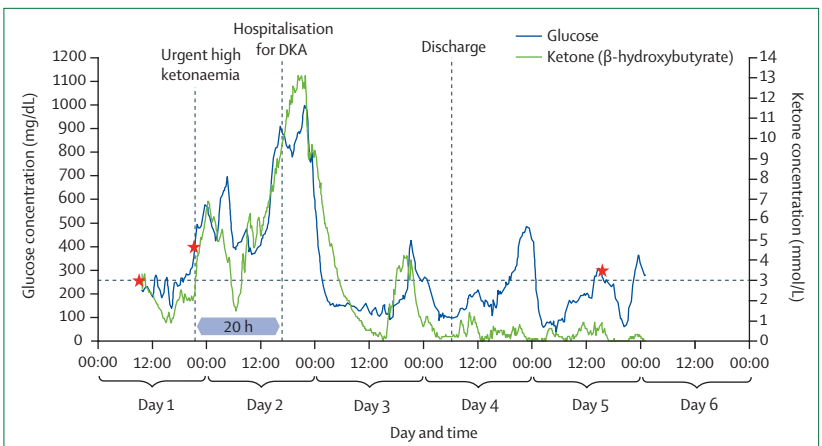

Figure 1: **Case study in continuous ketone monitoring**
A 14-year-old girl with type 1 diabetes was enrolled in a study using a blinded glucose/ketone sensor. She was advised to follow her standard method of diabetes management throughout the study. The sensor was applied on the back of the arm. The sensor was confirmed to be functioning, and she was released from clinic. Blinded glucose and ketone sensor data are represented in blue and green, respectively; the red stars represent capillary glucose measurements. An urgent high ketone level (≥3·0 mmol/L) was measured 20 h before hospitalisation with full clinical symptoms of DKA. The resolution of DKA can be seen with the initiation of an insulin drip following admission, with a slight elevation in glucose and ketones towards the end of the treatment period, which probably reflects the transition off the drip before discharge. This case illustrates how a continuous ketone monitor can follow ketonaemia and warn a person with diabetes to an impending episode of DKA, and conversely show resolution of ketosis. Case provided by Bruce Bode (Atlanta Diabetes Associates; personal communication). DKA=diabetic ketoacidosis.

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Panel: **Recommendations for application of continuous ketone monitoring devices in people with diabetes**

Each of the following recommendations have been assigned a level of supporting evidence (A [clear evidence from randomised controlled trials], B [supportive evidence from well conducted controlled studies], C [supportive evidence from poorly controlled or uncontrolled studies], or E [expert consus or clinical experience]), that adheres to the evidence-grading system of the American Diabetes Association Standards of Medical Care in Diabetes (appendix p 6).[26]

Recommendations on continuous ketone monitoring technology for manufacturers and regulators

- Continuous ketone monitoring devices must meet rigorous minimum accuracy and performance standards compliant with regulatory authorisation for use as medical devices for consistent ketone measurement in individuals with diabetes: B
- These standards must include accuracy and performance of continuous ketone monitoring sensors at differing rates of ketone change: B
- To have relevance in the context of changing ketone concentrations, visible trend arrows associated with continuous ketone monitoring functionality should reflect rates of ketone change of 0·4 mmol/L per h, to provide feedback of immediate value to the user (appendix p 7): E
- Manufacturers of continuous ketone monitoring devices used in the clinical management of people with diabetes are expected to make data that they collect from continuous ketone monitoring users available for health-care research: E

Recommendations on ketone monitoring threshold for health-care professionals

- Ketonaemia as measured by continuous ketone monitoring devices is the same, whether used by a person with type 1 diabetes or type 2 diabetes: C
- The recommended terminology for ketone concentrations at which continuous ketone monitoring users are advised to take action (figure 1) are normal, elevated, high and urgent high: C
- For all continuous ketone monitoring users the ketone concentrations associated with each threshold are: C:
  - Normal <0·6 mmol/L
  - Elevated 0·6 to 1·5 mmol/L
  - High >1·5 to <3·0 mmol/L
  - Urgent High ≥3·0 mmol/L
- Actions that continuous ketone monitoring users are advised to take at elevated, high and urgent high ketone concentrations (figure 1) are solely based on the ketone concentration displayed on the continuous ketone monitoring device and should be followed, irrespective of the associated trend arrow: E
- Advice provided by health-care professionals when contacted by continuous ketone monitoring users (figure 2) can consider the rate and direction of ketone trend arrows: E
- All health-care professionals involved in the care of people with diabetes using continuous ketone monitoring devices should be provided with clinical education and professional development specific to understanding the implications of changing ketone concentrations as indicated by continuous ketone monitoring technology, and aligned with international or national guidance on diabetic ketoacidosis avoidance or management: B

Use of continuous ketone monitoring in daily practice for people with diabetes

- To avoid potential alarm fatigue, it is recommended that continuous ketone monitoring devices have optional ketone threshold alarms, and used at the discretion of the user and their health-care professional: C
- It is recommended that an audible or vibrating alarm should be put in place to notify continuous ketone monitoring users if their ketone concentrations rise above the urgent high threshold of ≥3·0 mmol/L: C
- To minimise the risk of anxiety as a consequence of increased awareness of ketone concentrations, all continuous ketone monitoring users should be provided with education and awareness that clarifies the meaning of elevated ketones and specific actions that can be taken in response to ketonaemia: E
- Individuals provided access to continuous ketone monitoring devices should also be provided with capillary-blood ketone testing meters and test strips, along with education on how to use effectively when necessary: A
  - If symptoms of elevated, high or urgent high ketonaemia are not matched by continuous ketone monitoring readings, a capillary blood fingerstick ketone test should be done: B

Euglycaemic DKA, glucose below the 11·0 mmol/L (200 mg/dL) diagnostic threshold, was previously estimated to be 3% of cases in type 1 diabetes[31] but is emerging as a more-common event in special populations at risk of DKA, including during pregnancy[32] and in treatment with SGLT2 inhibitors.[33,34] Cases of DKA, including euglycaemic DKA, have been reported with use of GLP-1 receptor agonists in individuals with type 1 diabetes on insulin pump therapy.[35,36] Euglycaemic DKA can also lack the typical symptoms of hyperglycaemia, such as polydipsia and polyuria, with little evidence of volume depletion, thus increasing the need for clinical advice in association with CKM technology that does not reference symptoms or signs of hyperglycaemia.

Ketone concentrations in individuals with or without diabetes, what is normal?

Guidelines for ketone monitoring in individuals treated with SGLT2-inhibitors advise concern if β-hydroxybutyrate concentrations are greater than

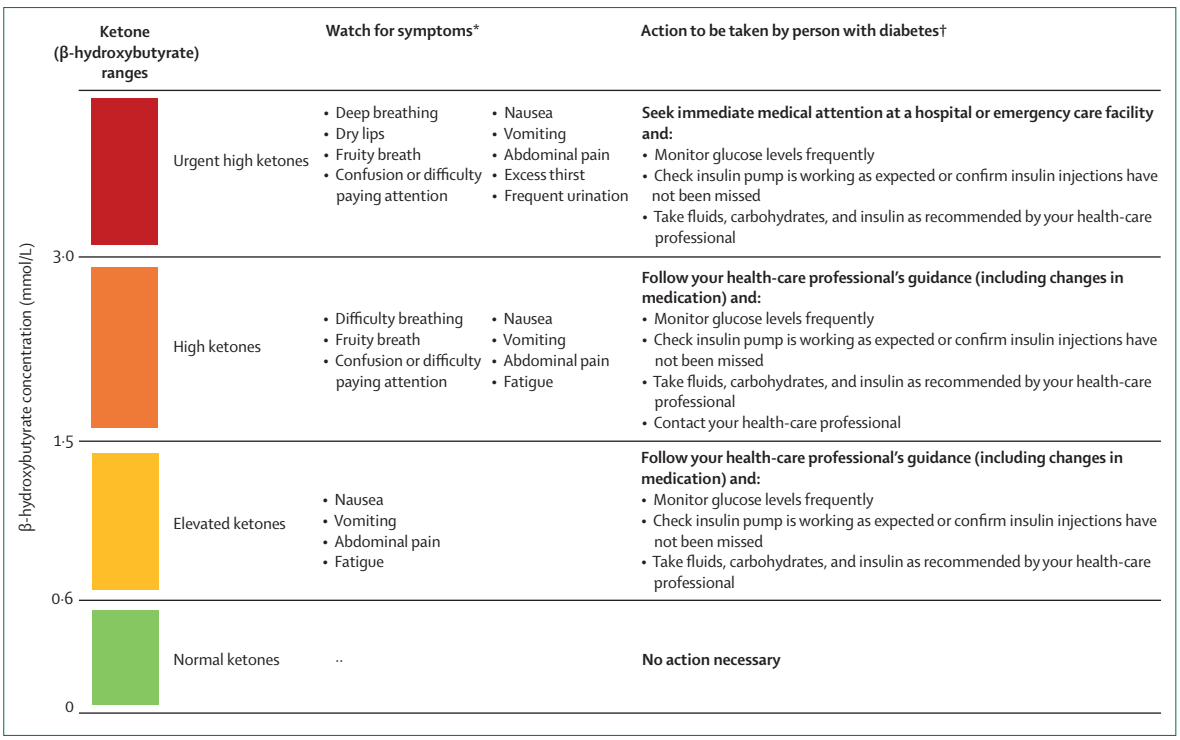

Figure 2: **Template schema for developing practical recommendations on continuous ketone monitoring thresholds**
*If continuous ketone monitoring readings do not match symptoms then perform a capillary blood ketone test. †See appendix (p 5) for possible action-based recommendations for health-care professionals to consider as part of possible clinical decision support functionality.

0·6 mmol/L, despite insufficient formal evidence.[37] People without diabetes have different ketone responses in different situations (appendix p 3). Children aged 3 years or younger can have mean β-hydroxybutyrate concentrations of 0·4 mmol/L, compared with 0·2 mmol/L in children aged 4–18 years,[38] and β-hydroxybutyrate concentrations of 1.0 mmol/L or higher are uncommon in these age groups (detected in 2% of individuals without diabetes). There is little evidence in people without diabetes that shows that older adults (>65 years) have a heightened ketogenic response to fasting or ketogenic diets, compared with younger adults.[39,40] In the absence of intercurrent illness, β-hydroxybutyrate concentrations of 0·06–0·20 mmol/L are observed following an overnight fast in adults (18 years or older) without diabetes (appendix p 3).[41,42] Ketogenic dieting, which includes greatly reducing carbohydrate intake, can see β-hydroxybutyrate concentrations rise to as high as 8·0 mmol/L in people without diabetes (appendix p 3), and studies on prolonged 7-day fasting in individuals with type 1 diabetes (n=19) indicate that β-hydroxybutyrate concentrations can rise to 2·8 mmol/L without adverse effects,[43] if insulin therapy is maintained. Starvation ketosis, with considerably elevated β-hydroxybutyrate concentrations, occurs with prolonged reduced intake of carbohydrate, typically meaning less than 500 kcal per day.[44] After several days of starvation, β-hydroxybutyrate concentrations can reach more than 5 mmol/L, compared to less than 3·0 mmol/L in a non-starvation state. Decreased food intake is also a component of alcoholic ketoacidosis, in which high consumption of alcohol combines with depletion of glycogen stores and ethanol-induced depression of gluconeogenesis, leading to β-hydroxybutyrate concentrations of 5·7–6·5 mmol/L on hospital admission.[45,46]

Applying the benefits of continuous ketone monitoring

Among people with diabetes there are groups who have an increased risk of DKA and in whom the symptoms, clinical management, and outcomes of DKA can differ from well established patient profiles (table 2). Application of CKM technology can be emphasised in these groups. A high priority will be in people with recurrent DKA, which represent as many as 22% of adults and children with diabetes who have a DKA event,[47,48] and is also more common in older and frail adults with diabetes.[54] These individuals have a larger burden of disease[63] and a disproportionate use of health-care resources.[49] CKM technology is also likely to have an immediate effect for people with diabetes on treatment with SGLT2 inhibitors, in whom DKA risk is elevated[33,34] and in whom euglycaemic DKA is more common.[34] Euglycaemic DKA is also more prevalent in women with diabetes during pregnancy than in women with diabetes

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See **Online** for appendix

	Risk association
Recurrent DKA	>20% of all DKA hospitalisations,[47,48] disproportionately greater use of health-care resources (eg, costs for hospital admission and treatment)[49]
SGLT2-inhibitor treatment	Elevated DKA risk compared with other glucose-lowering agents; associated with higher rates of euglycaemic DKA[32,33]
Pregnant women with pregestational diabetes or gestational diabetes	Increased insulin resistance; associated with higher rates of euglycaemic DKA[32]
Insulin pump users, including AID users	Increased risk of DKA due to catheter occlusion and insulin restriction[50–52]
Low carbohydrate or ketogenic diet	Can be exacerbated with SGLT2 inhibitors[53]
Older and frail individuals	Recurrent DKA more common[54]
Young adults with type 1 diabetes	Transitioning from paediatric to adult care, with reduced frequency of clinical review and specialised care access[55,56]
Rural populations	Remote from major health-care services and can have socioeconomic depravation, with reduced access to health-care services compared with urban populations, particularly specialist care[57,58]
Comorbid mental health disorders	Lower insulin adherence and association with antipsychotic medications[59,60]
Chronic kidney disease	Declining renal function associated with increased risk of DKA at lower ketone concentrations[61]
History of cardiovascular disease or advanced neuropathy associated with foot ulcers or amputation	3-fold (cardiovascular disease) and 1·5-fold (neuropathy) increased risk of DKA for people with type 1 diabetes[62]

The table lists defined groups of people with heightened risks for DKA. The list order indicates potential priorities for application once continuous ketone monitoring technology is approved for use as a medical device. AID=automated insulin delivery. DKA=diabetic ketoacidosis.

Table 2: **Subgroups of people with diabetes at heightened risk of diabetic ketoacidosis**

who are not pregnant.[32,64] Insulin pump therapy is also associated with increased risk of DKA, including with automated insulin delivery (AID) systems, as a consequence of infusion-set or infusion-site failures.[50–52,65] Clinical management of people with diabetes and obesity who are on low carbohydrate or ketogenic diets should also be facilitated by CKM devices because of their DKA risk, particularly if using SGLT2 inhibitors.[53] Longitudinal data show that people with type 1 diabetes and a history of cardiovascular disease, foot ulcers, or amputations are at greater risk of DKA.[62] Other at-risk populations include individuals with chronic kidney disease,[61] or heart failure.[66,67] Risks for DKA are also higher in rural populations,[57,58] in adolescents and young adults with type 1 diabetes,[55,56] and for adults with comorbid mental health or psychiatric illnesses compared with individuals in urban areas, older adults, and those with diabetes and no comorbid mental health illnesses (table 2).[59,60]

Episodic use of CKM can be appropriate in some of these groups, but the comparative value of episodic versus continuous use is an evidentiary gap, requiring data from real-world application of CKM systems. The potential use of CKM in any high-risk population also emphasises the need for health-care professional education in this regard, particularly since many of these high-risk groups can be managed in primary care (panel).

The evidence for ketone concentrations of concern in diabetes

The level of evidence for using a ketone concentration of 3·0 mmol/L as a diagnostic threshold for DKA is acknowledged to be low, graded as C (panel; appendix p 6) in the 2022 International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines,[2] and has been adopted on the basis of two studies. The first, a small study in 14 adults (mean age 41 years) with type 1 diabetes presenting with DKA at a hospital in Oxford, UK,[68] recommended a 3·0 mmol/L threshold for medical treatment based on measured rates of change in β-hydroxybutyrate concentrations of up to 1·8 mmol/L per h. With this rate of change, acidosis could be detected within 2–5 h of breaching the 3·0 mmol/L threshold. A larger study[30] undertook a retrospective review of medical records from a single hospital in the USA across 466 DKA admissions in children (n=129) and adults (n=337), for whom serum β-hydroxybutyrate and bicarbonate concentrations were both tested on admission. The study found that for children and adolescents aged younger than 16 years, a cutoff of 3·0 mmol/L or higher was appropriate to the diagnosis of DKA with bicarbonate concentration of 18 mmol/L, as reflected in the ISPAD guidelines, and that for individuals aged 16 years or older (termed adults in the study) the threshold was 3·8 mmol/L or higher, corresponding to a bicarbonate concentration of 18 mmol/L. The age cutoff in this study was based on an assessment that persons aged younger than 16 years have lower extracellular buffering capacity than older individuals.[69]

A 2023 study used the aforementioned outcomes to test the correlation between ketone concentrations—as measured by a capillary blood strip meter, and bicarbonate concentrations—with measurable acidosis (outcomes are shown in the appendix (p 4).[70] This study also reported that reducing the diagnostic β-hydroxybutyrate threshold of concern to ≥1·6 mmol/L identified 97·4% of episodes with bicarbonate concentrations of 18 mmol/L or less. This cutoff also identified 39·3% of episodes with bicarbonate concentrations of higher than 18 mmol/L.

Importantly, these data align with international guidance indicating that a β-hydroxybutyrate concentration of 1·6 mmol/L is the cutoff threshold for elevated concern regarding ketosis that requires treatment.[37] Evidence also indicates that diabetes type did not influence differences in β-hydroxybutyrate concentrations and correlations with bicarbonate or pH levels, and ketosis-prone adults with type 2 diabetes presenting with DKA have similar β-hydroxybutyrate concentrations as individuals with type 1 diabetes.[71–73]

A single-centre study in 504 adults with DKA admitted between 2006 and 2016 reported that renal function was a factor in the levels of β-hydroxybutyrate associated with bicarbonate and pH values in the acidotic range.[74] Individuals with end-stage kidney disease and eGFR lower than 15 mL/min per 1·73 m² had mean β-hydroxybutyrate concentrations of 4·3 mmol/L, associated with mean bicarbonate levels of 13·9 mmol/L and pH of 7·2; whereas individuals with moderate renal failure (eGFR 15–60 mL/min per 1·73 m²) had mean β-hydroxybutyrate 5·6 mmol/L, and individuals with preserved renal function (eGFR >60 mL/min per 1·73 m²) had mean β-hydroxybutyrate 5.9 mmol/L, and each had similar bicarbonate and pH levels as those with end-stage kidney disease. These results suggest that, for adults, ketone concentrations of concern could be lower for individuals with poorer renal function and lower eGFR.

Support for β-hydroxybutyrate monitoring is provided by a 6 month, multicentre randomised controlled trial of sick day management in 123 children and young adults, aged 3–22 years, comparing urine versus capillary blood ketone monitoring.[75] This study showed that β-hydroxybutyrate monitoring with capillary blood test strips was significantly better at reducing DKA risks, compared with urine acetoacetic acid testing.

In summary, serum β-hydroxybutyrate concentrations are correlated with bicarbonate concentrations and blood pH in people with type 1 diabetes and are diagnostic for DKA with high sensitivity and specificity. However, the evidence for an equivalence of a β-hydroxybutyrate concentration of 3·0 mmol/L with a bicarbonate concentration of 18 mmol/L or a blood pH of lower than 7·3 is not well supported in adults. Rather, the equivalence could be higher, at around 4.3 mmol/L (appendix p 4), and could vary dependent on renal function. For children and adolescents aged younger than 16 years with type 1 diabetes, the equivalence of a β-hydroxybutyrate concentration of 3·0 mmol/L with a bicarbonate concentration of 18 mmol/L is more supportable, but the evidence is scarce and there is no indication that age-dependent alert thresholds are safe or necessary (panel).

Interpreting ketone concentrations in the context of trend arrows

A key factor in the positive effect of CGM technology has been the trend arrows,[76] which accompany each glucose reading and provide information on the direction and the rate of glucose changes. Data show that trend arrows provide important feedback, allowing users to make informed choices regarding their immediate actions.[77–79] The incorporation of trend arrows in CKM technology has the potential to inform how ketone concentrations and thresholds can be interpreted and what actions might be recommended. The expert group felt that, to have relevance for changing ketone concentrations, visible trend arrows would need to reflect rates of change of around 0·4 mmol/L per h to provide feedback of immediate value to the user (panel). At this point in time, due to lack of clinical data it is not possible to conclude whether ketone trend arrows can have a role in interpreting different levels of concern or modifying associated actions (panel).

Mitigating alarm fatigue

Alarm fatigue has been reported as the most common factor in the discontinuation of use of CGM devices.[80–82] The same phenomenon can be anticipated for users of CKM technology, indicating that alerting thresholds should be set and managed to minimise potential alarm fatigue, which could be achieved with alerts that are both optional and customisable for each user, based on their own experience and in agreement with their health-care provider (panel). While acknowledging the importance of individualisation of care using CKM devices, it is recommended that an alarm should be set to notify users if their ketone concentrations rise to the threshold of 3·0 mmol/L or higher (panel).

Ketone thresholds, symptom awareness, and actions

A recommendation for ketone thresholds with escalating levels of concern and actions, based on CKM data, is provided in figure 2. The use of a traffic-light progression reinforces the increasing urgency of rising ketone concentrations and the need for action. A traffic-light display is also accepted as part of CGM reporting, which will help to build familiarity amongst users, caregivers, and health-care professionals with CGM experience, who progress to using CKM technology. The schema shown in figure 2 makes a connection between the concentration of CKM-reported ketones with awareness of any symptoms of ketonaemia and then with actions that the CKM user is advised to take. In the absence of data on how application of CKM might additionally inform interpretation of ketone thresholds and actions, these proposed thresholds and actions largely reflect current guidance[37] and take a cautious approach. For example, when using a CKM sensor, the cutoff for urgent action (red) is at a concentration of 3·0 mmol/L or higher, with alert zones of >0·6 to 1·5 mmol/L (yellow) and >1·5 to <3·0 mmol/L (orange) to provide information and actions that can be important in specific situations or in specific groups of

people with diabetes and heightened risks for DKA (table 2).

On the basis of future clinical research and real-world use of CKM devices, optional alerts for ketone concentrations lower than 3·0 mmol/L, other than 1·5 mmol/L, might be justified. In this context, a real-life case study has been published, which differs from that described in figure 1. It described an adult with type 1 diabetes, on an AID device and using a CKM sensor as part of a RCT investigating risk of DKA with SGLT2-inhibitor therapy.[52] Elevated ketone concentrations were detected by CKM at 1·0 mmol/L via an alert mandated by the RCT protocol, and continued to rise, with an upward trend arrow, despite actions aimed at ketone management using the AID settings. After rising past 3·1 mmol/L, as indicated by the CKM sensor, a capillary blood ketone test confirmed a ketone concentration of 3·7 mmol/L. On investigation, a dislodged pump cannula was replaced, and ketonaemia was treated using insulin and resolved. The individual remained asymptomatic throughout, but the episode confirmed the value of CKM to provide early awareness of ketonaemia for a person with type 1 diabetes, ultimately aiding in timely resolution of the episode without symptoms of DKA or hospital admission.

Research has also confirmed that routine ketone testing, outside of illness, can identify individuals who are at higher future risk of DKA, based on observed maximum ketone levels of 0·8 mmol/L or higher during regular fasting periods without illness.[83] These data suggest that CKM devices, in addition to identifying imminent risk of DKA, could also identify individuals with ketone patterns indicating a higher risk of future DKA, by more often reaching thresholds above the accepted normal range. Understanding the percentage of time with ketones in distinct ranges could help identify individuals with risks for recurrent DKA and prompt preventive strategies, such as more regular clinical visits, optimised basal insulin doses, and renewed education around precipitating factors. However, in the absence of sufficient CKM data, the positive predictive value of elevated ketone concentrations in the absence of precipitating factors cannot be known.

The recommended terminology for escalating ketone concentrations agreed by the consensus group is normal, elevated, high, and urgent high (figure 2), to emphasise the objective information on ketone concentrations and to link the data to levels of action. This terminology differs from more-functional language associated with increasing ketone concentrations based on urine or capillary blood tests, for example, none, trace, small, moderate, large. CKM technology can be predicted to provide the opportunity to understand the daily percentages of time spent with ketones at different concentrations, similar to the now-agreed targets for clinical metrics of time in range for glucose as measured by CGM devices.[84] The consensus group therefore recommends that CKM device manufacturers make the user data that they collect available for health-care research (panel).

The greater level of detail in the clinical advice provided in the appendix (p 5) is aimed at health-care professionals,[85] who could be contacted by a CKM user, following the visible information that accompanies a change in alert threshold (figure 2). There is no reason to propose that CKM use requires adjunct confirmation with a capillary blood strip test. However, if symptoms of elevated, high, or urgent high ketonaemia are not matched by CKM readings (figure 1), then a capillary blood ketone test can be done, and all CKM users should be provided with a ketone meter and test strips for this purpose (panel).

Education and awareness are key for continuous ketone monitoring

Increased awareness of ketone concentrations for CKM users should not be accompanied by increased anxiety, as this could increase disease burden for the person with diabetes and might prompt unnecessary calls to heath-care professionals. Therefore, the consensus group has recommended to provide ketone-specific education for all individuals who initiate CKM technology, including what elevated ketones mean and what actions to take (figure 2), to reiterate and extend education already provided to people with newly diagnosed type 1 diabetes during insulin initiation, or with transition to insulin pump therapy. This education should also be provided to all CKM users not taking insulin, particularly those at high risk for DKA (table 2), and for individuals in whom episodic rather than continuous application of CKM sensors could be recommended.

Effective application of ketone thresholds, as described, also requires that all health-care professionals managing people with diabetes receive appropriate clinical education (panel). CKM devices will increase awareness of changing ketone levels for users which might potentially be related to daily activities and in the absence of symptoms. This awareness is likely to increase the number of interactions that users initiate with their family physicians and primary care health-care professionals (figure 1), which will require knowledgeable advice in response, including what action to take.

Evidence gaps

The implementation of CKM technology is a pivotal moment in the evolution of diabetes technology, anticipated to improve outcomes for people with diabetes and generate data that will underpin future clinical guidelines. Currently, theres is no evidence on the natural daily fluctuations in ketone concentrations for a person with diabetes. CKM profiles that identify individuals at greater future risk of DKA need to be established. Many of the ketogenic stressors that apply to people without diabetes also apply for people with diabetes, and CKM data from cohorts of all individuals with diabetes across

the spectrum of daily activities must be collected. There is also a need for large cohort studies in which β-hydroxybutyrate concentrations, bicarbonate concentrations, and blood pH are all measured within a coincident timeframe for individuals with suspected DKA. Large studies will allow the equivalence between CKM-measured β-hydroxybutyrate concentrations with bicarbonate and pH levels to be conclusively mapped across different ages and with different diabetes medication regimens. Data on the lag times for appearance of β-hydroxybutyrate in interstitial fluid are also an important unmet need for use and interpretation of CKM data.

Fundamental to generating these data, and ensuring user safety, is to ensure rigorous regulatory compliance with assessment and performance standards that preclude the approval of CKM sensors for use as medical devices with insufficiently validated accuracy and precision data (panel). As with CGM systems, users could soon have a choice of CKM devices, and each of them should meet minimum performance standards. Meeting accuracy standards is an active issue within European regulatory structures for CGM devices[86] and must be addressed for all diabetes technologies.

Strengths and limitations

A limitation of the expert panel discussions and recommendations is the paucity of available evidence for use of CKM technologies in people with or without diabetes and the scarcity of clear evidence on physiological blood ketone profiles during daily living with or without diabetes. There is a lack of real-world data and clinical experience with CKM in people with diabetes outside of research settings, which is a limitation in this Personal View. Consequently, several recommendations are based on limited or preliminary evidence. Another limitation was that the selection of the expert panel was not systematised or randomised, rather it reflected clinical experience in diabetes technology and ketonaemia. A strength of the recommendations presented herein is that they are the outcomes of an acknowledged group methodology, involving brainstorming, discussion, and debate among health-care professionals with substantial expertise in the management of DKA in people with diabetes.

Search strategy and selection criteria

We searched MEDLINE, PubMed, and the Cochrane Library for research articles pertaining to physiological ketone concentrations and/or DKA in individuals with or without diabetes, published at any time up to Oct 24, 2025, by nested use of Boolean operators (AND/OR/NOT) to combine, expand or limit results, selectively. Terms used were: "randomized controlled trial", "randomized clinical trial", "real world study", "observational study", "cohort study", "continuous glucose monitoring", "ketone", "ketonemia", "ketosis", "acidosis", "diabetic ketoacidosis", "DKA", "type 1 diabetes", "type 2 diabetes", "continuous glucose monitoring", "continuous ketone monitoring", and "sick day rules". Randomised clinical trials, real world studies, observational studies, and cohort studies were included; case studies and case series were excluded. Studies published up to Oct 24, 2025 were included. Articles published in languages other than English, and studies in animals, were excluded.

Conclusion

A crucial element in the safe and effective use of CKM devices will be expert recommendations on alerting thresholds and actions that are appropriate to the realities of reducing risks for DKA, while avoiding alarm fatigue. There is a paucity of evidence to indicate how ketone thresholds can be best adapted to this new technology and it is likely that the application of CKM systems will provide the data that fill these gaps.

Contributors

KD, RMB, and TD wrote the first draft of the manuscript for discussion and debate. Subsequently, all authors contributed to the interpretation of key concepts and supporting research over serial drafts of the final manuscript. KD, RMB, and TD are the guarantors of this work and take responsibility for the integrity of the data analysis. All authors had access to all the data, and have reviewed, helped to revise, and approved the final version of this manuscript, and had final decision to submit for publication.

Declaration of interests

KD has received payment for lectures and consulting from Abbott, Boehringer Ingelheim, Eli Lilly, Roche Diabetes Care, Sanofi, and AstraZeneca; support for attendance at participation in speakers' bureaus for Abbott; and was sponsored by Breakthrough T1D to attend the writing group meetings for this manuscript. RMB has received grants or contracts from Abbott, DexCom, Eli Lilly, Embecta, Insulet, Medtronic, Novo Nordisk, Roche Diabetes Care, Tandem Diabetes Care, and Sanofi; consulting fees from Abbott, DexCom, Eli Lilly, Embecta, Novo Nordisk, Roche Diabetes Care, and Sanofi; payment or honoraria from Abbott, DexCom, Novo Nordisk, and Roche Diabetes Care; and support for attending meetings from Abbott, Dexcom, Eli Lilly, Novo Nordisk, and Roche Diabetes Care. RMB's employer, the non-profit HealthPartners Institute, contracts for his services and he receives no personal income from any of these activities. MA-S has received research support from Medtronic and Sanofi; served on advisory panels for Medtronic, Insulet, Abbott, VitalAire, Sanofi, and Dexcom; received honoraria for speaking from Abbott, Eli Lilly, Medtronic, Novo Nordisk, Sanofi, and VitalAire; received support from Medtronic for meeting attendance; and is the Vice President of the Saudi Society of Endocrinology and Metabolism and the Vice President of the Saudi Type 1 Diabetes Association. AA-O'N declares her employer receives grant support from Abbott, Medtronic, Sanofi, Novo Nordisk, and Vertex. TB declares that the institutions he works for (University of Ljubljana and University Children's Hospital–University Medical Centre Ljubljana) has received grants or contracts from Abbott, Medtronic, Novo Nordisk, Sanofi, Novartis, Sandoz, Zealand Pharma, Slovenian Research and Innovation Agency, US National Institutes of Health, Breakthrough T1D, Helmsley Foundation, and the European Union. TB has received payment or honoraria from Eli Lilly, Novo Nordisk, Medtronic, Abbott, Sanofi, Dexcom, Aventis, AstraZeneca, and Roche; and has participated on a data safety monitoring board or advisory board for Novo Nordisk, Sanofi, Eli Lilly, AstraZeneca, Medtronic, Abbott, Roche, SAB Bio, Tandem, and Dexcom. CDB received support (for this manuscript) from Abbott and Indigo Diabetes; consulting fees from Abbott, AstraZeneca, Boehringer Ingelheim, Dexcom, Eli Lilly, Indigo Diabetes, Insulet, Medtronic, and Novo Nordisk; and payment or honoraria from Abbott, Eli Lilly and Novo Nordisk. SD is an employee of Breakthrough T1D, and declares that this institution has received payment or honoraria from AstraZeneca, Abbott, Biomedia, Bayer,

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CMat serves or has served on advisory panels for Abbott, Bayer, Biomea Fusion, Boehringer Ingelheim, Eli Lilly, Medtronic, Insulet, Novo Nordisk, Novartis, Roche, SAB Bio, Sanofi, and Vertex (financial compensation for these activities has been received by KU Leuven; and research support has been received by KU Leuven from Abbott, Dexcom, Novo Nordisk and Sanofi); serves or has served on a speakers bureau for Eli Lilly, Vertex, Roche, Dexcom, Abbott, Medtronic, Novo Nordisk, Insulet, and Sanofi (financial compensation for these activities has been received by KU Leuven); is president of the European Association for the Study of Diabetes and vice-president of the European Diabetes Forum (all external support of the European Association for the Study of Diabetes is on www.easd.org). EM has received payment or honoraria from Abbott Research, Bayer, Boehringer Ingelheim, Embecta, Corcept, Eli Lilly, Insulet, and Novo Nordisk. 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References

1 Umpierrez GE, Davis GM, ElSayed NA, et al. Hyperglycemic crises in adults with diabetes: a consensus report. *Diabetes Care* 2024; **47:** 1257–75.

2 Glaser N, Fritsch M, Priyambada L, et al. ISPAD clinical practice consensus guidelines 2022: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes* 2022; **23:** 835–56.

3 Dhatariya KK, Glaser NS, Codner E, Umpierrez GE. Diabetic ketoacidosis. *Nat Rev Dis Primers* 2020; **6:** 40.

4 Hodzic-Santor B, Colacci M, Raissi A, et al. Validation of the diagnostic accuracy levels of International Classification of Diseases, 10th revision codes for diabetic ketoacidosis: a multicentre, cross-sectional study of adults. *Can J Diabetes* 2024; **48:** 227–32.

5 Laffel L. Ketone bodies: a review of physiology, pathophysiology and application of monitoring to diabetes. *Diabetes Metab Res Rev* 1999; **15:** 412–26.

6 Maahs DM, Hermann JM, Holman N, et al, and the National Paediatric Diabetes Audit and the Royal College of Paediatrics and Child Health, the DPV Initiative, and the T1D Exchange Clinic Network. Rates of diabetic ketoacidosis: international comparison with 49,859 pediatric patients with type 1 diabetes from England, Wales, the US, Austria, and Germany. *Diabetes Care* 2015; **38:** 1876–82.

7 Benoit SR, Hora I, Pasquel FJ, Gregg EW, Albright AL, Imperatore G. Trends in emergency department visits and inpatient admissions for hyperglycemic crises in adults with diabetes in the US, 2006–2015. *Diabetes Care* 2020; **43:** 1057–64.

8 Stougaard EB, Amadid H, Søndergaard E, et al. Time trends in the incidence of diabetic ketoacidosis leading to hospital admission among adults with type 1 diabetes: a nationwide Danish register study. *Diabetes Care* 2023; **46:** 1897–902.

9 Lavens A, Crenier L, Block CD, et al. Initiative for quality promotion and epidemiology in diabetes. 2024. https://www.sciensano.be/nl/biblio/initiatief-voor-kwaliteitsbevordering-en-epidemiologie-bij-diabetes-iked-audit-12-gegevens-2021-2022 (accessed Oct 2, 2025).

10 Kalscheuer H, Seufert J, Lanzinger S, et al, and the DPV Initiative. Event rates and risk factors for the development of diabetic ketoacidosis in adult patients with type 1 diabetes: analysis from the DPV registry based on 46,966 patients. *Diabetes Care* 2019; **42:** e34–36.

11 Roussel R, Riveline J-P, Vicaut E, et al. Important drop in rate of acute diabetes complications in people with type 1 or type 2 diabetes after initiation of flash glucose monitoring in France: the RELIEF study. *Diabetes Care* 2021; **44:** 1368–76.

12 Karges B, Rosenbauer J, Holterhus P-M, et al, and the DPV Initiative. Hospital admission for diabetic ketoacidosis or severe hypoglycemia in 31,330 young patients with type 1 diabetes. *Eur J Endocrinol* 2015; **173:** 341–50.

13 Budhram DR, Bapat P, Bakhsh A, et al. Prognostic implications of diabetic ketoacidosis in adults on long-term mortality and diabetes-related complications. *Can J Diabetes* 2024; **48:** 462–70.e3.

14 Lacy ME, Gilsanz P, Eng C, Beeri MS, Karter AJ, Whitmer RA. Severe hypoglycemia and cognitive function in older adults with type 1 diabetes: the study of longevity in diabetes (SOLID). *Diabetes Care* 2020; **43:** 541–48.

15 Chen Y-K, Lai C-H, Wang N-K, et al. Association of diabetic ketoacidosis and retinopathy in patients with type 2 diabetes: a nationwide cohort study. *Sci Rep* 2025; **15:** 33594.

16 Wysham C, Bindal A, Levrat-Guillen F, Kostadinova D, Poon Y. A systematic literature review on the burden of diabetic ketoacidosis in type 2 diabetes mellitus. *Diabetes Obes Metab* 2025; **27:** 2750–67.

17 Dhatariya K. Blood ketones: measurement, interpretation, limitations, and utility in the management of diabetic ketoacidosis. *Rev Diabet Stud* 2016; **13:** 217–25.

18 Larsson CR, Januszewski AS, McGrath RT, et al. Suboptimal behaviour and knowledge regarding overnight glycaemia in adults with type 1 diabetes is common. *Intern Med J* 2018; **48:** 1080–86.

19 Hepprich M, Roser P, Stiebitz S, et al. Awareness and knowledge of diabetic ketoacidosis in people with type 1 diabetes: a cross-sectional, multicenter survey. *BMJ Open Diabetes Res Care* 2023; **11:** e003662.

20 Albanese-O'Neill A, Wu M, Miller KM, Jacobsen L, Haller MJ, Schatz D, and the T1D Exchange Clinic Network. Poor adherence to ketone testing in patients with type 1 diabetes. *Diabetes Care* 2017; **40:** e38–39.

21 Cherubini V, Scaramuzza AE, Agrimi U, et al, and the Diabetes Study Group of the Italian Society for Pediatric Endocrinology and Diabetology. Initial observations on the frequency of diabetic ketoacidosis following pilot screening for type 1 diabetes in the general Italian population. *Diabetes Obes Metab* 2025; **27:** 6039–43.

22 Minerba E, Maines E, Quaglia N, et al. Diabetes awareness campaigns to prevent ketoacidosis at the diagnosis of type 1 diabetes: efficacy on multiple outcomes and predictors of success: a systematic review. *J Pers Med* 2024; **14:** 1115.

23 Alva S, Castorino K, Cho H, Ou J. Feasibility of continuous ketone monitoring in subcutaneous tissue using a ketone sensor. *J Diabetes Sci Technol* 2021; **15:** 768–74.

24 Nguyen KT, Xu NY, Zhang JY, et al. Continuous ketone monitoring consensus report 2021. *J Diabetes Sci Technol* 2022; **16:** 689–715.

25 Kong YW, Morrison D, Lu JC, Lee MH, Jenkins AJ, O'Neal DN. Continuous ketone monitoring: exciting implications for clinical practice. *Diabetes Obes Metab* 2024; **26** (suppl 7): 47–58.

26 American Diabetes Association Professional Practice Committee. 7. Diabetes technology: standards of care in diabetes—2025. *Diabetes Care* 2025; **48** (suppl 1)**:** S146–66.

27 Kovacs A, Bunduc S, Veres DS, et al. One third of cases of new-onset diabetic ketosis in adults are associated with ketosis-prone type 2 diabetes—a systematic review and meta-analysis. *Diabetes Metab Res Rev* 2024; **40:** e3743.

28 Jensen ET, Stafford JM, Saydah S, et al. Increase in prevalence of diabetic ketoacidosis at diagnosis among youth with type 1 diabetes: the SEARCH for diabetes in youth study. *Diabetes Care* 2021; **44:** 1573–78.

29 Eeg-Olofsson K, Nathanson D, Spelman T, et al. Initiation of intermittently scanned continuous glucose monitoring is associated with reduced hospitalization for acute diabetes events and cardiovascular complications in adults with type 1 diabetes. *Diabetes Care* 2024; **47:** 2164–71.

30 Sheikh-Ali M, Karon BS, Basu A, et al. Can serum β-hydroxybutyrate be used to diagnose diabetic ketoacidosis? *Diabetes Care* 2008; **31:** 643–47.

31 Macfarlane J, Dhatariya K. Incidence of euglycemic diabetic ketoacidosis in adults with type 1 diabetes in the United Kingdom before the widespread use of sodium glucose cotransporter 2 inhibitors. *Mayo Clin Proc* 2019; **94:** 1909–10.

32 Stathi D, Lee FN, Dhar M, et al. Diabetic ketoacidosis in pregnancy: a systematic review of the reported cases. *Clin Med Insights Endocrinol Diabetes* 2025; **18:** 11795514241312849.

33 Taylor SI, Blau JE, Rother KI. SGLT2 inhibitors may predispose to ketoacidosis. *J Clin Endocrinol Metab* 2015; **100:** 2849–52.

34 Blau JE, Tella SH, Taylor SI, Rother KI. Ketoacidosis associated with SGLT2 inhibitor treatment: analysis of FAERS data. *Diabetes Metab Res Rev* 2017; **33:** e2924.

35 Sharma PP, Ramirez-Berlioz AM, Weisz AD. Diabetic ketoacidosis in a patient With type 1 diabetes treated with a closed-loop sensor-augmented insulin infusion system. *AACE Clin Case Rep* 2023; **9:** 116–21.

36 Widhalm C, Pulido V. Euglycemic diabetic keto acidosis in a type 1 diabetic patient after glucose like peptide-1 administration: a case presentation. *J Investig Med High Impact Case Rep* 2023; **11:** 23247096231206333.

37 Danne T, Garg S, Peters AL, et al. International consensus on risk management of diabetic ketoacidosis in patients with type 1 diabetes treated with sodium-glucose cotransporter (SGLT) inhibitors. *Diabetes Care* 2019; **42:** 1147–54.

38 Parmar K, Mosha M, Weinstein DA, Riba-Wolman R. Fasting ketone levels vary by age: implications for differentiating physiologic from pathologic ketotic hypoglycemia. *J Pediatr Endocrinol Metab* 2023; **36:** 667–73.

39 London ED, Margolin RA, Duara R, et al. Effects of fasting on ketone body concentrations in healthy men of different ages. *J Gerontol* 1986; **41:** 599–604.

40 Freemantle E, Vandal M, Tremblay Mercier J, Plourde M, Poirier J, Cunnane SC. Metabolic response to a ketogenic breakfast in the healthy elderly. *J Nutr Health Aging* 2009; **13:** 293–98.

41 Anfinsen ÅM, Myklebust VH, Johannesen CO, et al. Serum concentrations of lipids, ketones and acylcarnitines during the postprandial and fasting state: the postprandial metabolism (PoMet) study in healthy young adults. *Br J Nutr* 2024; **132:** 851–61.

42 Burstal RJ, Reilly JR, Burstal B. Fasting or starving? Measurement of blood ketone levels in 100 fasted elective and emergency adult surgical patients at an Australian tertiary hospital. *Anaesth Intensive Care* 2018; **46:** 463–67.

43 Berger B, Jenetzky E, Köblös D, et al. Seven-day fasting as a multimodal complex intervention for adults with type 1 diabetes: Feasibility, benefit and safety in a controlled pilot study. *Nutrition* 2021; **86:** 111169.

44 Cahill Jr GF. Fuel metabolism in starvation. *Annu Rev Nutr* 2006; **26:** 1–22.

45 Umpierrez GE, DiGirolamo M, Tuvlin JA, Isaacs SD, Bhoola SM, Kokko JP. Differences in metabolic and hormonal milieu in diabetic- and alcohol-induced ketoacidosis. *J Crit Care* 2000; **15:** 52–59.

46 Wrenn KD, Slovis CM, Minion GE, Rutkowski R. The syndrome of alcoholic ketoacidosis. *Am J Med* 1991; **91:** 119–28.

47 Mays JA, Jackson KL, Derby TA, et al. An evaluation of recurrent diabetic ketoacidosis, fragmentation of care, and mortality across Chicago, Illinois. *Diabetes Care* 2016; **39:** 1671–76.

48 Hammersen J, Tittel SR, Warncke K, et al, and the DPV Initiative. Previous diabetic ketoacidosis as a risk factor for recurrence in a large prospective contemporary pediatric cohort: results from the DPV initiative. *Pediatr Diabetes* 2021; **22:** 455–62.

49 Lyerla R, Johnson-Rabbett B, Shakally A, Magar R, Alameddine H, Fish L. Recurrent DKA results in high societal costs—a retrospective study identifying social predictors of recurrence for potential future intervention. *Clin Diabetes Endocrinol* 2021; **7:** 13.

50 Marks BE, Meighan S, Fivekiller EE, Escobar E, Berget C. Ketone management in pediatric diabetes centers in the USA: current practices and a call for improved standardization. *Horm Res Paediatr* 2024; published online Oct 15. https://doi.org/10.1159/000541430.

51 Pala L, Dicembrini I, Mannucci E. Continuous subcutaneous insulin infusion vs modern multiple injection regimens in type 1 diabetes: an updated meta-analysis of randomized clinical trials. *Acta Diabetol* 2019; **56:** 973–80.

52 Kong YW, Jones HC, Ngan J, et al. Preventing diabetic ketoacidosis with continuous ketone monitoring: insights from a clinical research case. *Diabetes Technol Ther* 2025; published online July 24. https://doi.org/10.1177/15209156251362494.

53 Roberts CGP, Athinarayanan SJ, Ratner RE, Umpierrez GE. Illnesses associated with ketosis including diabetic ketoacidosis during very low carbohydrate and ketogenic diets. *Diabetes Obes Metab* 2025; **27:** 2531–39.

54 Masuda S, Ota K, Okazaki R, et al. Clinical characteristics associated with the development of diabetic ketoacidosis in patients with type 2 diabetes. *Intern Med* 2022; **61:** 1125–32.

55 Ebrahimi F, Kutz A, Christ ER, Szinnai G. Lifetime risk and health-care burden of diabetic ketoacidosis: a population-based study. *Front Endocrinol* 2022; **13:** 940990.

56 Holman N, Woch E, Dayan C, et al. National trends in hyperglycemia and diabetic ketoacidosis in children, adolescents, and young adults with type 1 diabetes: a challenge due to age or stage of development, or is new thinking about service provision needed? *Diabetes Care* 2023; **46:** 1404–08.

57 Chepulis L, Papa V, Lao C, et al. Epidemiology of diabetic ketoacidosis in the Waikato region of New Zealand: 2000–2019. *J Diabetes Res* 2023; **2023:** 4715783.

58 Kao KT, Lei S, Cheek JA, White M, Hiscock H. Paediatric diabetes-related presentations to emergency departments in Victoria, Australia from 2008 to 2018. *Emerg Med Australas* 2024; **36:** 101–09.

59 Berger G, Waldhoer T, Barrientos I, et al. Association of insulin-manipulation and psychiatric disorders: a systematic epidemiological evaluation of adolescents with type 1 diabetes in Austria. *Pediatr Diabetes* 2019; **20:** 127–36.

60 Scheuer SH, Andersen GS, Carstensen B, et al. Trends in incidence of hospitalization for hypoglycemia and diabetic ketoacidosis in individuals with type 1 or type 2 diabetes with and without severe mental illness in Denmark from 1996 to 2020: a nationwide study. *Diabetes Care* 2024; **47:** 1065–73.

61 Stathi D, Dhatariya KK, Mustafa OG. Management of diabetes-related hyperglycaemic emergencies in advanced chronic kidney disease: review of the literature and recommendations. *Diabet Med* 2025; **42:** e15405.

62 Bapat P, Budhram DR, Bakhsh A, et al. Longitudinal determination of diabetes complications and other clinical variables as risk factors for diabetic ketoacidosis in type 1 diabetes. *Diabetes Care* 2025; **48:** 614–22.

63 Garrett CJ, Choudhary P, Amiel SA, Fonagy P, Ismail K. Recurrent diabetic ketoacidosis and a brief history of brittle diabetes research: contemporary and past evidence in diabetic ketoacidosis research including mortality, mental health and prevention. *Diabet Med* 2019; **36:** 1329–35.

64 Eshkoli T, Barski L, Faingelernt Y, Jotkowitz A, Finkel-Oron A, Schwarzfuchs D. Diabetic ketoacidosis in pregnancy—case series, pathophysiology, and review of the literature. *Eur J Obstet Gynecol Reprod Biol* 2022; **269:** 41–46.

65 Hughes MS, Douvas JL, Layfield-Bryan M, et al. Frequency and detection of insulin infusion site failure in the Type 1 Diabetes Exchange Online Community. *Diabetes Technol Ther* 2023; **25:** 426–30.

66 Alroobi H, Dargham S, Mahfoud Z, Jayyousi A, Al Suwaidi J, Abi Khalil C. Diabetic ketoacidosis and hyperosmolar hyperglycemic state in diabetes patients with heart failure: insight from the National inpatient sample. *BMC Cardiovasc Disord* 2025; **25:** 384.

67 Tecce N, de Alteriis G, de Alteriis G, et al. Harnessing the synergy of SGLT2 inhibitors and continuous ketone monitoring (CKM) in managing heart failure among patients with type 1 diabetes. *Healthcare* 2024; **12:** 753.

68 Wallace TM, Meston NM, Gardner SG, Matthews DR. The hospital and home use of a 30-second hand-held blood ketone meter: guidelines for clinical practice. *Diabet Med* 2001; **18:** 640–45.

69 Cassels DE, Morse M. Arterial blood gases and acid-base balance in normal children. *J Clin Invest* 1953; **32:** 824–36.

70 Kilpatrick ES, Butler AE, Saeed S, Alamuddin N, Atkin SL, Sacks DB. The effectiveness of blood glucose and blood ketone measurement in identifying significant acidosis in diabetic ketoacidosis patients. *Diabetol Metab Syndr* 2023; **15:** 198.

71 Jahoor F, Hsu JW, Mehta PB, et al. Metabolomics profiling of patients with A–β+ ketosis-prone diabetes during diabetic ketoacidosis. *Diabetes* 2021; **70:** 1898–909.

72 Ooi E, Nash K, Rengarajan L, et al. Clinical and biochemical profile of 786 sequential episodes of diabetic ketoacidosis in adults with type 1 and type 2 diabetes mellitus. *BMJ Open Diabetes Res Care* 2021; **9:** e002451.

73 Hirobata T, Inaba H, Kaido Y, et al. Serum ketone body measurement in patients with diabetic ketoacidosis. *Diabetol Int* 2022; **13:** 624–30.

74 Galindo RJ, Pasquel FJ, Vellanki P, et al. Biochemical parameters of diabetes ketoacidosis in patients with end-stage kidney disease and preserved renal function. *J Clin Endocrinol Metab* 2021; **106:** e2673–79.

75 Laffel LMB, Wentzell K, Loughlin C, Tovar A, Moltz K, Brink S. Sick day management using blood 3-hydroxybutyrate (3-OHB) compared with urine ketone monitoring reduces hospital visits in young people with T1DM: a randomized clinical trial. *Diabet Med* 2006; **23:** 278–84.

76 Zoccarato F, Manzoni M, Minotti D, Lettieri E, Boaretto A. Unveiling the interplay between rational, psychological and functional factors in continuous glucose monitoring early adoption: novel evidence from the Dexcom ONE case in Italy. *BMC Health Serv Res* 2024; **24:** 747.

77 Pettus J, Edelman SV. Recommendations for using real-time continuous glucose monitoring (rtCGM) data for insulin adjustments in type 1 diabetes. *J Diabetes Sci Technol* 2017; **11:** 138–47.

78 Klonoff DC, Kerr D. A simplified approach using rate of change arrows to adjust insulin with real-time continuous glucose monitoring. *J Diabetes Sci Technol* 2017; **11:** 1063–69.

79 Laffel LM, Aleppo G, Buckingham BA, et al. A practical approach to using trend arrows on the Dexcom G5 CGM system to manage children and adolescents with diabetes. *J Endocr Soc* 2017; **1:** js.2017-00389-. https://doi.org/10.1210/js.2017-00389.

80 Farfel A, Liberman A, Yackobovitch-Gavan M, Phillip M, Nimri R. Executive functions and adherence to continuous glucose monitoring in children and adolescents with type 1 diabetes. *Diabetes Technol Ther* 2020; **22:** 265–70.

81 Cobry EC, Vigers T, Berget C, et al. Frequency and causes of nocturnal alarms in youth and young adults with type 1 diabetes using a first-generation hybrid closed-loop system. *Diabetes Spectr* 2024; **37:** 118–23.

82 Barnard-Kelly KD, Martínez-Brocca MA, Glatzer T, Oliver N. Identifying the deficiencies of currently available CGM to improve uptake and benefit. *Diabet Med* 2024; **41:** e15338.

83 Song C, Dhaliwal S, Bapat P, et al. Point-of-care capillary blood ketone measurements and the prediction of future ketoacidosis risk in type 1 diabetes. *Diabetes Care* 2023; **46:** 1973–77.

84 Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the International Consensus on Time in Range. *Diabetes Care* 2019; **42:** 1593–603.

85 Goldenberg RM, Gilbert JD, Hramiak IM, Woo VC, Zinman B. Sodium-glucose co-transporter inhibitors, their role in type 1 diabetes treatment and a risk mitigation strategy for preventing diabetic ketoacidosis: the STOP DKA protocol. *Diabetes Obes Metab* 2019; **21:** 2192–202.

86 Mathieu C, Irace C, Wilmot EG, et al. Minimum expectations for market authorization of continuous glucose monitoring devices in Europe—'eCGM' compliance status. *Diabetes Obes Metab* 2024; **27:** 1025–31.