

Provincial Clinical Knowledge Topic
*Diabetic Ketoacidosis, Adult
Emergency Department*

Topic Title:	Diabetic Ketoacidosis, Adult Emergency Department	Creation Date:	September 2015
Clinical Working Group:	Emergency SCN – Diabetic Ketoacidosis	Revised Date:	March 2016
Status:	Approved	Version:	1.1

Version	Date	Revision	Revised By
1.1	March 2016	Table 1, PICO Question 4 & 8 updated Small wording change in Medications under Insulin	Dr Lyle Thomas Dr Michael Bullard Karin Domier Sarah Searle Erin Hayward

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Important Information Before You Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Health Now campaign etc.

Within this knowledge topic PICO-D questions or key clinical questions that have been used to guide research using the **P**opulation/**P**roblem, **I**ntervention, **C**omparison, **O**utcome, **D**esign format. These questions are listed in Appendix A.

Links to PICO questions or Appendices are throughout the document (example: ([PICO 1](#)) or ([Appendix A](#))). Click on the link with your mouse to follow the link. Under the PICO question or Appendix heading you will find a link to return you to your place in the document.

Rationale

Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS) are the most commonly encountered diabetic decompensation emergencies. Both are caused by a relative or absolute deficiency of insulin and elevated levels of counter regulatory hormones. This ensuing hyperglycemia results in a combination of osmotic diuresis, electrolyte abnormalities and ketone production/acidosis that can lead to significant morbidity and mortality. In Canada, the incidence has been estimated at 4.6-8.0 per 1000 person-years resulting in 5000-10000 hospital admissions for DKA per year. The most common causes of diabetic decompensation are inadequate insulin treatment (including non-compliance), precipitating stressors (e.g. infection, cardiovascular insult, and trauma) and medications. As well, many undiagnosed diabetics' initial presentation will be that of DKA. The estimated mortality rate is between 4-10% per year for DKA and 10-50% per year for HHS, due to underlying medical conditions¹. Table 1 below illustrates the impact DKA has had on Alberta Emergency Departments in recent years, in terms of presentation and admission rates, and resulting resources that are used (Emergency Medical Services [EMS]). The fact that around 50% of mortality occurs in the first 48-72 hours reinforces the need to properly diagnose and begin correct management in the ED².

While there is no absolute definition for the diagnosis of DKA, it typically includes: hyperglycemia (blood glucose level greater than 14 mmol/L), venous pH less than 7.3 or bicarbonate less than 15 mmol/L, and ketonemia greater than or equal to 3 mmol/L or significant ketonuria (greater than 2+ on standard urine sticks) resulting in an increased anion gap.

The diagnosis of HHS typically includes altered mentation, severely elevated serum glucose, minimal or no ketonemia/ketonuria, elevated serum osmolality, arterial pH greater than 7.3 and bicarbonate greater than 15 mmol/L.

This document will outline the diagnosis and management of the **adult** DKA patient only. Pediatric patients require special considerations that are not outlined in this document and therefore it should not be used as a guideline in pediatric cases.

Table 1. Diabetic Ketoacidosis Emergency Visits 2012 – 2014^a

Zone	ED Visits	# Admits	% Admits	# by EMS	% by EMS	# Transfer to Another Acute Site	%Transfer to Another Acute Site
Calgary	785	712	90.7%	412	52.5%	4	0.5%
Central	147	113	76.9%	71	48.3%	1	0.7%
Edmonton	698	587	84.1%	333	47.7%	7	2.4%
North	156	130	83.3%	51	32.7%	0	0.0%
South	125	116	92.8%	44	35.2%	0	0.0%
Grand Total	1911	1658	86.8%	911	47.7%	22	1.2%

^aData provided by AHS Data Integration, Management and Reporting (DIMR)³

Click here for the expanded table: [Diabetic Ketoacidosis Emergency Room Visits Site Detail](#)

Goals of Management

1. ABC: Protect airway, support ventilation, volume resuscitate as needed
2. Differentiate diabetic ketoacidosis (DKA) from hyperosmolar hyperglycemic state (HHS) based on appropriate clinical and laboratory criteria
3. Identify and treat immediately life threatening conditions such as hypo/hyperkalemia
4. Rule out and treat co-existing/precipitating conditions such as sepsis, myocardial infarction, cerebrovascular accident (CVA), pancreatitis, drugs (corticosteroids, thiazides, sympathomimetics, and antipsychotic agents), etc.
5. Select appropriate resuscitation fluid based on clinical/laboratory criteria
6. Anticipate and prevent complications of treatment such as electrolyte abnormalities and cerebral edema
7. Manage associated signs and symptoms (e.g. abdominal pain, nausea and vomiting)
8. Monitor closely and adjust treatments depending on clearly defined clinical and laboratory endpoints (e.g. urine output, rate of serum glucose decline, repeat potassium/ketone levels)
9. Continue management until appropriate endpoints reached (resolution of acidosis, patient tolerating oral intake)
10. Arrange appropriate admission based on disease severity (intensive care versus general medicine ward)
11. Provide safe and appropriate discharge planning and diabetic teaching

Nursing Assessment and Documentation

This section contains specific considerations related to this topic. Standard assessment and documentation practices should still be followed.

1. Triage Assessment:
 - Vital signs, including blood glucose measurement
 - Canadian Emergency Department Information Systems (CEDIS) complaint: Hyperglycemia
Note: Patients may also present to the Emergency Department (ED) with another CEDIS presenting complaint such as Altered Level of Consciousness, Hyperventilation, Chest pain, Abdominal pain, Vomiting and/or Nausea, or Fever
 - Canadian Triage and Acuity Scale (CTAS) Modifiers: Blood sugar greater than 14 mmol/L & symptomatic or blood sugar greater than 14 mmol/L & asymptomatic are the most likely 2nd order/special modifiers; Respiratory distress, Hemodynamic, or Level of consciousness as most likely 1st order modifiers; and Dehydration as a possible 2nd order/special modifier⁴

2. Initial Assessment/Documentation:

- Presenting History:
 - Polyuria, polydipsia, weight loss, nausea/vomiting, abdominal pain, weakness, mental status change, coma
- Past History:
 - Previous episodes of DKA
- Medications/Allergies:
 - Include regular insulin dosing schedule if appropriate
- Systems review:
 - Vital Signs (VS): including bedside glucose monitoring (capillary blood glucose [CBG])
 - Respiratory: tachypnea, Kussmaul respirations, dyspnea, smell of ketones on breath
 - Cardiovascular: tachycardia, hypotension, signs dehydration, diaphoresis, chest pain
 - Neurological: neuro VS, seizure activity, irritability, decreased level of consciousness (LOC), confusion, focal neurologic complaints, vision changes, coma
 - Gastrointestinal: nutrition status, nausea, vomiting, abdominal pain
 - Genitourinary: recent urine output
 - Other: fever, decreased skin turgor

3. Ongoing Assessment/Documentation:

- The following parameters should be monitored and documented (nursing flow sheet) on an ongoing basis while in the ED:
 - Vital signs/CBG
 - Neurologic status/Glasgow Coma Scale (GCS)
 - Ins and Outs (Genitourinary and Gastrointestinal)
 - Other: e.g. Pain scale

Physician Assessment and Documentation

This section contains specific considerations related to this topic. Standard assessment and documentation practices should still be followed.

1. History of Present Illness:

- Include signs and symptoms of precipitating causes (e.g. sepsis, acute coronary syndrome [ACS], and cerebrovascular accident [CVA])

2. Past History:

- Includes past episodes of DKA and patient's normal diabetic control

3. Review of Systems:

- Look for signs and symptoms of precipitating causes
4. Social History:
- History of substance abuse (e.g. alcohol, intravenous drug use)
 - Ability to be compliant with follow up care (e.g. lives alone, no fixed address)
5. Physical Examination:
- Focused exam looking for diagnosis (dehydration/Kussmaul breathing/acetone smell), severity (hypovolemic shock/decreased LOC), precipitating causes (infection/myocardial infarction [MI]/CVA/other acute pain presentation/trauma)

Initial Decision Making – Stable vs. Unstable; DKA vs HHS

1. Is the patient **hemodynamically unstable** with their hyperglycemic emergency?
- If yes, priorities include:
 - Restoration of normal extracellular fluid volume (ECFV) and tissue perfusion
 - IV 0.9% NaCl 1 to 2 L/hour until shock corrected (**PICO 1**) then:
 - IV 0.9% NaCl 500 mL/hour for 4 hours, then 250 mL/hour for 4 hours
 - Recommended maximum of 50 mL/kg over first 4 hours
 - Assessment and appropriate correction of life threatening electrolyte imbalance (e.g. hypo/hyperkalemia) (**PICO 2**)
 - Appropriate control of severe acidosis (**PICO 3**)
 - Insulin required to correct acidosis (**PICO 4**)
 - Bicarbonate recommended only for pH less than 7.0 after adequate fluid resuscitation
 - Be aware of potential complications if airway management is required:
 - Effect of Rapid Sequence Intubation (RSI) medications on serum potassium (e.g. succinylcholine)
 - Effect of respiratory rate/hypoventilation in severe acidosis
2. Is the patient **hemodynamically stable** with their hyperglycemic emergency?
- If yes, priorities include:
 - Restoration of normal extracellular fluid volume (ECFV) and tissue perfusion (**PICO 5**)
 - IV 0.9% NaCl 500 mL/hour for 4 hours, then 250 mL/hour for 4 hours
 - Suggest change IV solution to 0.45% NaCl at above rate if:
 - Patient euvolemic or mild hypovolemia (HR less than 100, SBP normal for patient, normal respiratory rate/mental status/capillary refill time, urine output greater than 0.5 mL/kg/hour)⁵
 - Corrected Na⁺ greater than 135 mmol/L
 - Plasma osmolality is falling less than 3 mmol/hour
 - Recommended maximum of 50 mL/kg over first 4 hours
 - Assessment and appropriate correction of electrolyte imbalance
 - Add potassium immediately if the patient is normo- or hypokalemic

- If hyperkalemic add potassium once it falls to less than 5.3 mmol/L
 - Appropriate control of severe acidosis
 - Insulin required to correct acidosis
 - Once serum glucose less than 15 mmol/L change IV fluids to D5W-0.45% NaCl with potassium chloride at a rate of 150 or 250 mL/hour to maintain plasma glucose of 12 – 14 mmol/L and continue insulin infusion until acidosis corrected. ([PICO 6](#))
 - Bicarbonate recommended only for pH less than 7.0 after adequate fluid resuscitation
3. Determine whether DKA or HHS ([PICO 7](#))
- HHS often higher glucose level and more profound fluid deficit
 - For HHS, change IV solution to 0.45% NaCl once hypotension corrected as long as osmolality is falling less than 3 mmol/hour
4. Is there an identifiable precipitating cause for the DKA/HHS?
- Common causes include:
 - New diagnosis of diabetes
 - Insulin omission
 - Infection
 - Myocardial infarction
 - Thyrotoxicosis
 - Drugs
5. Does the patient have signs of complications associated with treatment of DKA/HHS?
- Complications to try to avoid include:
 - Hyper/hypokalemia
 - ECFV overexpansion
 - Cerebral edema
 - Hypoglycemia

Order Set Components

Orders or their components have been added in **bold** text if recommended as default. All other orders would be selected based on the presentation needs of the patient. Orders that have more than one option for treatment have been entered in square brackets (e.g. warfarin 5 mg [2, 2.5, 3, 4, 6, 7.5, 10 mg] PO x 1).

Order Set Components - General Care

- Goals of Care: Goals of Care Designation, while relevant to all presentations this is less likely to be known or something to address on presentation in patients with DKA
- Precautions and Safety:
 - Consider universal precautions/isolation if communicable infectious cause suspected
- Activity:
 - **Bedrest**
 - Bedrest - With bathroom privileges
 - Activity as Tolerated
- Restraints – Mechanical: Soft physical restraints can be a consideration to keep patients with altered level of consciousness in a side lying position for safety
- Diet / Nutrition:
 - **NPO**
 - NPO - May Take Oral Medications With Sips
 - NPO - May Have Ice Chips
 - Clear Fluids
 - Diabetic Diet as tolerated
 - Other diets: as required

Order Set Components - Patient Care Orders

- Vital Signs, suggest starting with ‘as per local nursing standards’ as the default with specified options for patients that physicians have a heightened level of concern about. These orders need to be re-evaluated when the patient stabilizes or in 2 hours whichever occurs first. Vital signs to include: respiratory rate (RR), pulse rate (P), blood pressure (BP), temperature (T), and oxygen saturation (O2 Sat) with options to include:
 - **as per local standards**
 - manual or automatic
 - q __ hour(s)
 - q __ minutes
- Bedside glucose monitoring (capillary blood glucose [CBG]), suggest start by measuring hourly
 - Option to lengthen interval as patient stabilizes (e.g. q1 [2,4] hour)
- Neurological vital signs may be indicated and include,
 - Glasgow Coma Scale (GCS), and pupillary size and reaction to light with reassessments,
 - **as per local standards**
 - q __ hour(s)
 - q __ minutes

- Note: the physician should be notified if a patient's GCS decreases by two points or more.
- Continuous cardiac monitoring, suggested if any of following conditions exist and a monitored bed is available:
 - Unstable vital signs
 - Severe hyper/hypokalemia with ECG changes
 - Suspected Acute Coronary Syndrome as precipitating cause
 - Physician discretion
- Ins and Outs
 - Measure and record output (+/- input) [q 1,2,4] hour; Notify physician if output less than 0.5 mL/kg/hour
 - Foley catheter as per physician order

Order Set Components - Respiratory Care

- Note: physician should be notified if O2 flow required to be increased by greater than 2 L to maintain the same level of oxygenation or if there is a progressive increase in the work of breathing
- O2 Therapy – Titrate to Saturation greater than or equal to 92%, unless otherwise specified
- O2 Therapy: @ ___ L / min via ___ to maintain O2 sat greater than or equal to ___

Order Set Components - Intravenous Orders

- Intravenous Cannula - Insert 1 or 2 large bore as required
- Intraosseous Cannula, acceptable initially if unable to get intravenous access
- Saline lock
- IV 'bolus' or 'rapid infusion' including the following:
 - Amount (i.e. 250 mL, 500 mL, 1000 mL, 2000 mL)
 - Fluid (i.e. **0.9% NaCl infusion**, 0.45% NaCl, D5W-0.45% NaCl)
 - Run time (i.e. 15 min, 30 min, 45, min, 60 min)
- IV 'maintenance'
 - Rate in mL / hour (i.e. 75, 100, 125, 150, 200, 250, 500)
 - Fluid (i.e. **0.9% NaCl infusion**, 0.45% NaCl, D5W-0.45% NaCl)
 - Duration (i.e. 1, 2, 4 hours then reassess)
- Most DKA patients are total body potassium depleted at presentation. Once diuresis is established, potassium should be added to IV solution based on serum potassium values:
 - Serum K⁺ greater than 5.2 mmol/L: HOLD potassium
 - Serum K⁺ 3.3 – 5.2 mmol/L: add potassium chloride 20 mmol/L to each 1 Litre bag of fluid
 - Serum K⁺ less than 3.3 mmol/L:
 - HOLD insulin until K⁺ greater than 3.3 mmol/L AND
 - add potassium chloride 20 to 40 mmol to each 1 litre bag of fluid

- NOTE: Maximum rate of K⁺ administration is 20 mmol/hour. For example, 1 Litre of Normal Saline with 40 mmol of potassium chloride should run at 500 mL/hour max rate.
- Consider using potassium phosphate instead of potassium chloride if severe hypophosphatemia
- When serum glucose less than 15 mmol/L change IV fluids to D5W-0.45% NaCl with potassium chloride at a rate of 150 or 250 mL/hour to maintain plasma glucose of 12 to 14 mmol/L and continue insulin infusion until acidosis corrected.

Order Set Components - Lab Investigations

Laboratory orders appear in **bold** text if recommended as usual default orders. Laboratory orders are underlined when needed to assess severity or establish a baseline. All other lab orders (e.g. investigations for possible comorbidities) are to be selected based on the presentation needs of the patient and are in regular font.

- Hematology
 - **Complete Blood Count (CBC)**
 - D-dimer
- Chemistry
 - **Electrolytes (Na, K, Cl, CO₂)**
 - **Glucose Random LEVEL**
 - **Creatinine LEVEL**
 - **Urea**
 - Phosphate LEVEL
 - Osmolality
 - Serum b-OHB (PICO 8)
 - Hemoglobin A1c
 - Magnesium (Mg) LEVEL
 - Calcium (Ca) LEVEL
 - Troponin
 - Lipase
 - HCG Beta
- Blood Gases
 - Blood Gas Venous
 - Blood Gas Arterial
- Microbiology
 - Blood Culture
- Urine Tests
 - Urinalysis
 - Urine Culture

- Pregnancy Test, Urine
- Special Fluids
 - Cerebrospinal fluid (CSF) analysis

Comments regarding laboratory ordering and utilization for this patient group;

1. The anion gap (AG) can be calculated as, $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$ with a normal range of 4 -12 mmol/L. An elevated gap in this population should lead clinicians to consider diabetic ketoacidosis.
2. The osmol gap (OG) is calculated as the difference between measured serum osmolality and calculated osmolality. Calculated osmolality = $2 \times \text{Na}^+ + \text{glucose} + \text{Urea}$ (all measured in mmol/L). A normal gap is less than 10 mOsm/kg. Both ketones and lactate will contribute to an osmolar gap.
3. Serum electrolytes should initially be ordered every 2-4 hours until anion gap and bicarbonate levels normal and electrolyte abnormalities resolve.
4. If glucose level too high for Point of Care testing (POCT), serum glucose levels should be ordered every 1-2 hours until readable on bedside monitors to allow for insulin infusion adjustments

Order Set Components - Diagnostic Investigations

- Standard X-rays
 - GR Chest, 2 Projections (Chest X-ray PA and Lateral)
 - GR Chest, 1 Projection portable (Chest X-ray Portable)
 - If clinical concern of precipitating cause (Pneumonia, CHF)
- Advanced imaging (e.g. Ultrasound or CT Scan)
 - If clinical concern of precipitating cause
 - Use IV contrast with caution when required if renal compromise or patient on metformin (hold for 48 hours post contrast injection)
- Electrocardiogram (ECG) - 12 lead
 - Identifies severe electrolyte abnormalities as well as potential precipitating cause (acute coronary syndrome [ACS])

Order Set Components - Medications

- Insulin
 - Short acting insulin (Humulin R/ Novolin ge Toronto) 0.1 [0.15] units/kg/hour IV until serum glucose less than 15 mmol/L and then reassess ([PICO 9](#))
 - Goal is to reduce serum glucose by 10% per hour or 2 to 4 mmol/L/hour. If not reducing adequately then increase (double) the current insulin infusion rate or provide a bolus dose of insulin (0.1 to 0.15 unit/kg of Humulin R/Toronto). If decline is too rapid, then decrease (halve) current insulin infusion rate.

- Insulin infusion should be continued until acidosis corrected (as assessed by pH/serum bicarbonate level/anion gap). If serum glucose less than 15 mmol/L change IV fluids to D5W-0.45% NaCl (with potassium chloride at concentration described below) at 150 or 250 mL/hour and adjust insulin infusion to maintain plasma glucose of 12 to 14 mmol/L. Continue insulin infusion until acidosis corrected.
 - Patients with continuous subcutaneous insulin pumps should have them discontinued and initiate IV insulin infusion as outlined above instead.
 - Subcutaneous insulin should be initiated once acidosis resolved and patient tolerating oral diet
 - Maintain IV insulin infusion for 2 hours after subcutaneous dose given to prevent rebound hyperglycemia
- Potassium (**PICO 2**)
 - Serum K⁺ greater than 5.2 mmol/L: HOLD potassium
 - Serum K⁺ 3.3 to 5.2 mmol/L: add potassium chloride 20 mmol/L to each 1 Litre bag of fluid
 - Serum K⁺ less than 3.3 mmol/L:
 - HOLD insulin until K⁺ greater than 3.3 mmol/L AND
 - add potassium chloride 20 to 40 mmol/L to each 1 Litre bag of fluid
- Sodium Bicarbonate (**PICO 3**)
 - Not recommended unless severe acidosis (pH less than 7.0) remains despite adequate fluid resuscitation
 - 1 ampoule (50 mmol) in 200 mL D5W infused over 1 hour
- Magnesium
 - 2 g IV over 1 to 2 hours as required
- Treat for precipitating causes as indicated (e.g. antibiotics, ASA, thrombolysis)

Order Set Components - Procedures, Policies & Guidelines

1. Physician

- Intubation under rapid sequence induction (RSI) (medication options: propofol, midazolam, fentanyl, ketamine, succinylcholine, rocuronium) (**PICO 10**)
- Central line access if required (+/- ultrasound guidance)
- Lumbar puncture if indicated (source of infection, decreased LOC)
- Incision and Drainage (I&D) any accessible abscess (source of infection)

2. Nursing

- Blood Glucose Monitoring (POCT) (1,2,4) hourly
- Measure and record output (+/- input) [1,2,4] hourly
- Monitor and adjust insulin infusion

- Monitor electrolytes and adjust accordingly

Disposition Planning

1. Considerations for admission

- Intensive Care unit (ICU) to be considered for patients with persistent severe acidosis, continuing altered LOC, hemodynamic instability or evidence of a critical care requirement inciting illness (e.g. severe sepsis, acute myocardial infarction) or secondary complication (e.g. cerebral edema, aspiration pneumonia with hypoxia).

[\(PICO 11\)](#)

- Patients presenting with significant acidosis (pH less than 7.2) significant dehydration (greater than 10% body weight loss⁶), or clear depletion of total body sodium or potassium should be admitted to a general ward until homeostasis is restored and their diabetic management reviewed and stabilized. Consider admission for all patients with new diagnosis of diabetes presenting in DKA.
- All patients with HHS should be admitted to stabilize and prevent secondary complications.

2. Considerations for discharge

- Patient presenting early with less severe DKA, minimal acidosis, hemodynamically stable, without the need for large volume fluid replacement and/or potassium supplementation can be considered for discharge. Prior to discharge the patient should be clinically well with stable glucose values, HCO₃ greater than 18, pH greater than 7.3 and have a clear understanding of their diabetic management regimen. Whenever possible, it is suggested to have primary care or a diabetic team member to follow up with in the next 1-2 days.
- Resolution of HHS is indicated by return to normal vital signs, normal serum osmolality and restored mentation.

3. Outpatient follow-up

- Where possible, for patients with a primary care physician, send a visit summary requesting the patient follow up with them. For patients with no primary care physician, having an alternate follow up option in the community is important.

4. Patient education / discharge instructions [\(Appendix C\)](#)

- Patient requires clear instructions for daily insulin administration regime. Also requires instructions for “sick days”
- Dietitian/Diabetes Education Center

Rural Considerations

1. Certain laboratory tests such as, osmolality, serum ketones and arterial blood gases are not universally available and for those cases where these tests would be important the attending physician may need to consult regional or urban referral centers, rather than send blood samples out for testing due to unnecessarily long delay in reporting turnaround times
2. Patients in rural centers that require intensive care monitoring or dedicated nursing assessments may not have capability/manpower to manage patient and require transfer to regional or urban referral centers
3. Patients requiring specialized care for precipitating cause may require transfer (acute coronary syndrome [ACS], cerebrovascular accident [CVA])

Patient Experience and Expectations

Based on a meeting with 8 patient advisors in Calgary January 25, 2015, we received the following feedback and general recommendations regarding approaches to communication, care and patient expectations in the emergency department (ED):

1. They hoped we would be able to improve care consistency among ED providers.

Patient quote: "Every time I presented to the emergency department with the same condition (atrial fibrillation), each doctor provided a different treatment approach."

2. They were supporters of care pathways, checklists, protocols, etc. wherever appropriate.

Patient quote: "I am a strong supporter of care pathways as whenever I/my family member receive treatment using a pathway the care seems clearer and more consistent"

3. While none of the patients liked long waits, they could accept them better if there was clearer communication and reassessments as required.

Patient quote: "Nobody likes to wait and I understand that sicker patients take priority, however, there needs to be improved communication and reassessments for those patients who are waiting"

4. They pointed out the importance of having a patient advocate accompany a sick person, but also allowing the advocate to be with the patient at decision critical points (e.g. initial assessment, treatment decision making, receiving bad news, etc.) was considered paramount.

Patient quote: "When I accompany my family member to the ED I am often not permitted to join them when they are moved into a treatment space. I am often told this is 'policy'."

5. They believe that improving follow up, especially for patients being discharged from the ED and being referred to a specialist is important. This was recognized as a key safety risk for patients; having to rely on faxed referrals and a call back from the consultant's office can lead to dangerous delays or failed connections to the detriment of the patient's health and well-being.

Patient quote: "The current health care system is poorly coordinated with lots of gaps and delays, especially with referrals from one physician to another."

Additional Clinical Decision Support (CDS) Considerations

Example:

Alert the clinician if a diabetic patient has a higher than previous glucose result returned. Comment: This 2nd alert such as high glucose OR med allergy OR incompatible med combination; these are "system" alerts that need to be generated based on a broad discussion to avoid 'alert' fatigue

Preparation for Analytics

1. Key Outcomes

- Clinical
 - Normal saline resuscitation of 500-1000 mL/hour provided in the first 2 hours
 - Sodium bicarbonate not given initially even if pH less than 7.0
 - Potassium given for all patients with potassium less than 5.3 mmol/L
- Process
 - Glucose, pH, +/- HCO₃ monitored hourly for 1st 4 hours
 - Ins and outs initiated early to track urine production
- Patient Experience
 - Felt supported when recovered enough to be aware of surroundings and able to begin to think clearly (timely explanation by staff of what had happened and what was going to happen which helped alleviate anxiety)
 - Provided with clear instructions and follow up if discharged

2. Data Elements for Capture

- Patient demographics
- CEDIS presenting complaint and CTAS score
- ED time markers (triage to physician, physician to consult and then to admission or physician to discharge) and outcome markers (identified as clinical decision unit patient, consulted for admission, admitted to intensive care unit or ward, deceased)
- ED diagnoses
- Site and zone identifiers
- Date and time of use of DKA order set
- Date and time of serum b-hydroxybutyrate, glucose and HCO₃
- Date and time and volume and type of IV fluids infused over the first 4 hours
- Date and time of insulin given over the first 4 hours
- Date, time, and dose of sodium bicarbonate given over the first 4 hours
- Date, time, and dose of potassium given over the first 4 hours

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Updated July 5, 2012.

Appendix A - PICO-D Questions (Key Clinical Questions)

For information regarding PICO-D Methodology and GRADE Terminology please see [Appendix B](#)

PICO 1: *In adult patients presenting to the ED with signs of dehydration and diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state (HHS) what is the preferred resuscitation fluid and preferred rate?*

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Population, Patient or Problem: Adults presenting with DKA or HHS

Intervention, Prognostic Factor, Exposure: Normal saline high vs low volume

Comparison: Alternate fluid high vs low volume

Outcome: successful resuscitation, sodium normalization, cerebral edema,

Design: Randomized Control Trials (RCTs) or Prospective Observational studies.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: We suggest that normal saline is the recognized resuscitation of choice with 0.45% saline initiated for patients with normal or elevated serum sodium levels.

While there are no systematic reviews available on resuscitation/rehydration for patients presenting to the ED with DKA or HHS, two non-systematic reviews^{1,2} identified several studies examining rehydration for patients with DKA and HHS. They recommend the following:

“In the absence of cardiac compromise, isotonic saline (0.9% NaCl) infused at a rate of 15-20 mL/kg/hr or 1-1.5 litres during the first hour. Subsequent choice for fluid replacement depends on hemodynamics, the state of hydration, serum electrolyte levels, and urinary output. In general, 0.45% NaCl infused at 250 –500 mL/hr is appropriate if the corrected serum sodium is normal or elevated; 0.9% NaCl at a similar rate is appropriate if corrected serum sodium is low. Successful progress with fluid replacement is judged by hemodynamic monitoring (improvement in blood pressure), measurement of fluid input/output, laboratory values, and clinical examination. Fluid replacement should correct estimated deficits within the first 24 hours. In patients with renal or cardiac compromise, monitoring of serum osmolality and frequent assessment should be considered.”

The American Diabetes Association recommends 0.9% saline of 15-20 mL/kg/hr³. If corrected serum sodium rises above 155 mmol/L, 0.45 % NaCl should be provided at a rate of 4-14 mL/kg/hr.

Quality of Evidence: Very Low, GRADE D.

Strength of Recommendation: Weak, GRADE 2

References:

1. Nyenwe EA, Kitabchi AE. Evidence-based management of hyperglycemic emergencies in diabetes mellitus. *Diabetes Res and Clin Pract.* 2011;94(3):340-351.
2. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care.* 2009;32(7):1335-1343.
3. American Diabetes Association. Hyperglycemic crises in patients with diabetes mellitus. *Diabetes Care.* 2003;26(suppl 1):S109–S117.

PICO 2: In adult patients presenting to the ED with diabetic ketoacidosis (DKA) when and how rapidly should potassium replacement be provided?

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Population, Patient or Problem: Adults presenting with DKA (with low vs normal or high potassium levels)

Intervention, Prognostic Factor, Exposure: Low potassium (adequate vs unknown renal function)

Comparison: Normal or high potassium (adequate vs unknown renal function)

Outcome: prevention of hypo/hyperkalemic complications, time to target potassium levels

Design: RCTs or Systematic reviews.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: While there is insufficient evidence to address the question, we do know that failure to recognize, prevent and treat hypokalemia is a significant mortality risk. No systematic reviews on diabetes and potassium replacement could be identified. Guidelines from the American Diabetic Association recommend that if serum potassium is less than 3.3 mmol/L, insulin should be held and give 40 mmol of potassium in each litre of IV fluid until serum potassium is equal to or greater than 3.3 mmol/L.¹ If serum potassium is equal or greater than 3.3 but less than 5.0 mmol/L, give 20-30 mmol potassium in each litre of IV fluid to keep serum potassium at 4-5 mmol/L. If potassium is equal or greater than 5.0 mmol/L, do not give potassium but check its levels every two hours. No time frame was given. De Beer et al recommends correcting serum potassium levels to 3-5 mmol/L before insulin is commenced, as insulin and saline will decrease extracellular serum levels². Potassium replacement should not occur if potassium levels are high (exceed 5.5 mmol/L)³.

Quality of Evidence: Very Low, GRADE D

Strength of Recommendation: Insufficient evidence

References:

1. American Diabetes Association. Hyperglycemic crises in patients with diabetes mellitus. *Diabetes Care*. 2003;26(suppl 1):S109–S117.
2. De Beer K, Michael S, Thacker M, et al. Diabetic ketoacidosis and hyperglycaemic hyperosmolar syndrome – clinical guidelines. *Nurs Crit Care*. 2008;13(1):5-1.
3. Keays R. Diabetic emergencies. In: Bernsten A, Oh TE, Soni N, eds. *Oh's Intensive Care Manual*, 5th ed. Oxford: Butterworth-Heinemann. 2003;551.

Additional Readings and General References:

Williams DR. Outcome indicators for diabetes services: what do we have and what do we need? *Community Med*. 1989;11(1):57–64.

PICO 3: In adult patients presenting to the ED with diabetic ketoacidosis (DKA) and severe acidosis what are the most effective treatments to normalize pH?

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Population, Patient or Problem: Adults presenting with DKA and severe acidosis (pH less than 7.0)

Intervention, Prognostic Factor, Exposure: IV insulin plus saline volume replacement

Comparison: Sodium bicarbonate

Outcome: time to pH normalization,

Design: Retrospective RCTs or Systematic reviews.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: There is insufficient evidence to make a definitive recommendation regarding the use of agents such as sodium bicarbonate to help normalize pH in an attempt to decrease morbidity in patients. Various small trials have failed to find a benefit or deleterious change in morbidity or mortality in providing sodium bicarbonate to patients with a pH < 7.0^{1,2,3,4}.

Despite this the American Diabetes association suggests that due to the well-known harmful effects of severe acidosis, patients with a pH of less than 6.9 should be provided with sodium bicarbonate added to 400 mL sterile water and given at a rate of 200 mL/hr¹. In patients with a pH of 6.9-7.0, 50 mmol sodium bicarbonate is diluted in 200 mL sterile water and infused at a rate of 200 mL/hr. Sodium bicarbonate should not be provided to patients with a pH over 7.0. Unclear if these suggestions apply to patients presenting to the ED.

Quality of Evidence: Low, GRADE C

Strength of Recommendation: Insufficient evidence

References:

1. American Diabetes Association. Hyperglycemic crises in patients with diabetes mellitus. *Diabetes Care*. 2003;26(suppl 1):S109–S117.
2. Duhon B, Attridge RL, Franco-Martinez AC, Maxwell PR, Hughes DW. Intravenous sodium bicarbonate therapy in severely acidotic diabetic ketoacidosis. *Ann Pharmacother*. 2013;47(7-8):970-975.
3. Lever E, Jaspán JB. Sodium bicarbonate therapy in severe diabetic ketoacidosis. *Am J Med*. 1983;75(2):263-268.
4. Viallon A, Zeni F, Lafond P, et al. Does bicarbonate therapy improve the management of severe diabetic ketoacidosis. *Crit Care Med*. 1999;27(12):2690-2693.

PICO 4: *In adult patients presenting to the ED with diabetic ketoacidosis (DKA) how should insulin be delivered?*

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Population, Patient or Problem: Adults presenting with DKA

Intervention: IV insulin

Comparison: SC insulin

Outcome: time to glycemia control, time to acidosis control

Design: RCTs or Systematic reviews.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: We suggest that insulin be provided via IV until the patient is showing clear signs of DKA resolution. Intravenous fluids are required as part of the management protocol and the intravenous route is preferred due to the short half-life of regular insulin and easy titration when compared to the delayed and prolonged half-life of subcutaneous regular insulin¹.

A recent Cochrane review, comparing SC insulin analogues to IV insulin in patients with mild, moderate, and severe DKA was published. It identified several randomized trials comparing SC insulin/insulin analogues and IV insulin in adult patients. Overall, in patients with mild-moderate DKA, SC insulin was found to be a safe and equally effective treatment option when compared to IV insulin^{2,3,4,5}.

Quality of Evidence: Moderate, GRADE B

Strength of Recommendation: Weak, GRADE 2

References:

1. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32(7):1335-1343.
2. Ersoz HO, Ukinc K, Kose M, et al. Subcutaneous lispro and intravenous regular insulin treatments are equally effective and safe for the treatment of mild and moderate diabetic ketoacidosis in adult patients. *Int J Clin Pract*. 2006;60(4):429-433.
3. Karoli R, Fatima J, Salman T, Sandhu S, Shankar R. Managing diabetic ketoacidosis in non-intensive care unit setting: Role of insulin analogs. *Indian J Pharmacol*. 2011;43(4):398-401.
4. Umpierrez GE, Latif K, Stoever J, et al. Efficacy of subcutaneous insulin lispro versus continuous intravenous regular insulin for the treatment of patients with diabetic ketoacidosis. *Am J Med*. 2004;117(5):291-296.
5. Umpierrez GE, Cuervo R, Karabell A, Latif K, Freire AX, Kitabchi AE. Treatment of diabetic ketoacidosis with subcutaneous insulin aspart. *Diabetes Care*. 2004;27(8):1873-1878.

Additional Readings and General References:

Andrade-Castellanos CA, Colunga-Lozano LE, Delgado-Figueroa N, Gonzalez-Padilla DA. Subcutaneous rapid-acting insulin analogues for diabetic ketoacidosis. *Cochrane Database Syst Rev*. 2014;(9):CD011281.

Fisher JN, Shahshahani MN, Kitabchi AE. Diabetic ketoacidosis: low-dose insulin therapy by various routes. *N Engl J Med*. 1977;297(5):238-241.

PICO 5: *In patients with special considerations who present in DKA, should fluid resuscitation be adjusted (e.g. known congestive heart failure, dialysis/renal failure patients)?*

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Population, Patient or Problem: Adult ED patients with confirmed DKA with special circumstances predisposing to fluid overload (CHF/renal failure)

Intervention, Prognostic Factor, Exposure: Lower total volume fluid resuscitation in first 4 hours

Comparison: High total volume fluid resuscitation in first 4 hours

Outcome: successful resuscitation, avoidance of pulmonary edema/cerebral edema

Design: RCTs, Cohort studies or Systematic reviews.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: There is insufficient evidence as no well-designed studies are available to answer this question. The American Diabetes association recommended that patients with renal or cardiac compromise, monitoring of serum osmolality and frequent assessment of cardiac, renal and mental status must be performed during fluid resuscitation to avoid iatrogenic

fluid overload¹. De Beer et al reported that the choice of replacement fluid should consider factors such as age, degree of hydration, and patient history² (e.g. cardiac disease). No details provided on how to adjust fluid resuscitation in patients with special consideration. Guidelines only report that serum osmolality should be monitored in patients with cardiac or renal compromise.

Quality of Evidence: Very Low, Grade D.

Strength of Recommendation: Insufficient evidence

References:

1. American Diabetes Association. Hyperglycemic crises in patients with diabetes mellitus. *Diabetes Care*. 2003;26(suppl 1):S109–S117.
2. De Beer K, Michael S, Thacker M, et al. Diabetic ketoacidosis and hyperglycaemic hyperosmolar syndrome – clinical guidelines. *Nurs Crit Care*. 2008;13(1):5-1.

PICO 6: In adult patients in the ED being managed for diabetic ketoacidosis (DKA) when should patients be switched to dextrose containing IV fluids?

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Population, Patient or Problem: Adults being managed for DKA with IV insulin and saline only

Intervention, Prognostic Factor, Exposure: IV insulin plus saline (N saline)

Comparison: IV insulin plus dextrose and saline (D5W)

Outcome: prevention of hypoglycemia, continued resolution of acidosis,

Design: RCTs or Systematic reviews.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: We suggest that during insulin therapy, once plasma glucose reaches 15 mmol/L, it may be possible to decrease the insulin infusion rate to 0.05-0.1 unit/kg/h (3-6 units/h), and 5-10% dextrose may be added to IV fluids¹. The goal of adding dextrose to IV replacement fluids at this stage is to maintain a plasma glucose level of 12mmol/L. This allows the continued administration of insulin until ketonaemia is controlled without the risk of hypoglycemia.

Quality of Evidence: Very Low, GRADE D

Strength of Recommendation: Weak, GRADE 2

References:

1. American Diabetes Association. Hyperglycemic crises in patients with diabetes mellitus. *Diabetes Care*. 2003;26(suppl 1):S109–S117.

Additional Readings and General References:

Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32(7):1335-1343

PICO 7: In adults patients presenting to the ED with hyperglycemia what are the differentiating features (clinical and lab) of DKA and HHS?

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Population, Patient or Problem: Adults presenting with hyperglycemia

Intervention, Prognostic Factor, Exposure: DKA findings

Comparison: HHS findings

Outcome: differentiating lab tests, timely recognition, appropriateness of management, adverse outcomes

Design: Cohort or Prospective Observational studies.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: There is insufficient evidence in the form of systematic reviews or trials to answer this question. The American Diabetes Association provided diagnostic criteria for DKA and HHS¹. Diagnostic criteria for HHS including plasma glucose of greater than 35 mmol/L, arterial pH of greater than 7.30, serum bicarbonate greater than 15 mmol/L, small urine and serum ketones, effective serum osmolality greater than 320 mOsm/kg, variable anion gap, and the patient is presenting in a stupor/coma regarding alteration in sensoria or mental obtundation. The diagnostic criteria for mild, moderate, and severe DKA includes plasma glucose of greater than 15 mmol/L, arterial pH ranging from less than 7.00 – 7.25, serum bicarbonate levels of less than 10-18 mmol/L, positive urine and serum ketones, variable effective serum osmolality, anion gap of greater than 10, and alteration in sensoria or mental obtundation ranging from alert (mild), alert/drowsy (moderate), and stupor/coma (severe).

Quality of Evidence: Very Low, GRADE D

Strength of Recommendation: Insufficient evidence. However, there are levels of consensus within textbooks or by diabetic organizations to help identify the differentiating features of DKA and HHS.

References:

1. American Diabetes Association. Hyperglycemic crises in patients with diabetes mellitus. *Diabetes Care*. 2003;26(suppl 1):S109–S117.

PICO 8: *In an undifferentiated adult ED patient with suspected DKA, is a serum b-hydroxybutyrate ketone measurement required to confirm the diagnosis?*

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Population, Patient or Problem: Undifferentiated adult ED patient with suspected DKA

Intervention, Prognostic Factor, Exposure: Serum b-hydroxybutyrate

Comparison: Hyperglycemia plus other evidence of acidosis

Outcome: diagnostic accuracy, impact on management, time to recovery

Design: Prospective or Cohort studies (using Reference standard +/- Receiver Operating Characteristic [ROC] curves)/metaanalyses.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: There is insufficient evidence and lack of consensus to make a recommendation regarding whether serum β -hydroxybutyrate ketone measurement is required to confirm DKA diagnosis in adults. While there is evidence to suggest that measuring serum β -hydroxybutyrate ketone may be as effective in identifying DKA as other tests, there was no evidence that it is necessary to confirm the diagnosis of DKA.

There are several non-randomized studies which have found that measuring β -hydroxybutyrate is effective in detecting DKA^{1,2}. Some studies have been published which have found measuring blood β -hydroxybutyrate useful. One cohort study did not find serum β -hydroxybutyrate testing to be sufficient in diagnosing ketoacidosis by itself in adults with uncontrolled diabetes mellitus³. Another cohort study found β -hydroxybutyrate testing to be as sensitive as other established tests in identifying DKA⁴.

Klocker et al conducted a systematic review comparing the use of testing blood β -hydroxybutyrate vs urine acetoacetate for the prevention and management of ketoacidosis in patients with type 1 diabetes⁵. Four studies (two RCT's and 2 cohort studies) including pediatric/young adults. A meta-analysis was not complete due to high heterogeneity. Overall, the blood β -hydroxybutyrate testing was associated with reduced frequency of hospitalization, shorter time to recovery from diabetic ketoacidosis, likely due to a more rapid diagnosis of DKA. Blood β -hydroxybutyrate testing was also associated with lower costs, and increased patient/caregiver satisfaction. This review only included studies assessing pediatric and young adults (less than or equal to 22 yrs old).

Quality of Evidence: Very Low, GRADE D

Strength of Recommendation: Insufficient evidence

References:

1. Bektas F, Eray O, Sari R, Akbas H. Point of care blood ketone testing of diabetic patients in the emergency department. *Endocr Res.* 2004;30(3):395-402.
2. Charles RA, Bee YM, Eng PH, Goh SY. Point-of-care blood ketone testing: screening for diabetic ketoacidosis at the emergency department. *Singapore Med J.* 2007;48(11):986-989.
3. Fulop M, Murthy V, Michilli A, Nalamati J, Qian Q, Sanitowitz A. Serum beta-hydroxybutyrate measurement in patients with uncontrolled diabetes mellitus. *Arch Intern Med.* 1999;159(4):381-384.
4. Naunheim R, Jang TJ, Banet G, Richmond A, McGill J. Point-of-care test identifies diabetic ketoacidosis at triage. *Acad Emerg Med.* 2006;13(6):683-685.
5. Klocker AA, Phelan H, Twigg SM, Craig ME. Blood β -hydroxybutyrate vs. urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review. *Diabet Med.* 2013;30(7):818-824.

PICO 9: In adult patients in the ED with DKA receiving a regular IV insulin infusion what targets/guidelines should be used to optimize the insulin dosing?

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Population, Patient or Problem: Adults with DKA on a infusion of regular IV insulin and saline only

Intervention, Prognostic Factor, Exposure: Continuous IV insulin in saline at 0.1 unit/kg/hr until DKA resolved

Comparison: IV insulin infusion doubling or halving based on rate of glucose correction

Outcome: time to DKA resolution, patient comfort and safety, continued resolution of acidosis,

Design: RCTs or Systematic reviews.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: We suggest that the American Diabetic association and Kitabchi et al recommendations that low dose insulin 0.1 units/kg/hr (5-7 units/h in adults) should be administered with the goal of decreasing serum glucose at a rate of 3-4 mmol/L the first hour are an appropriate standard^{1,2}. Serum glucose should be checked hourly. If serum glucose does not continue to fall, then the hourly insulin should be doubled until glucose falls at a steady hourly rate of 3-4 mmol/L.

De Beer et al suggested similar recommendations³. Intravenous insulin should be provided at 0.1 U/kg/hr, and serum glucose checked hourly. Blood glucose should not fall by more than 4 mmol/L per hour. If blood glucose falls by less than 3 mmol/L in the first hour, than the insulin dose needs to be doubled. When blood glucose reaches 12-14 mmol/L, halve the insulin rate. Titrate insulin to

maintain blood glucose of 4-10 mmol/L until DKA resolves and serum osmolality is less than 320 mOsmol/L

Quality of Evidence: Very Low, GRADE D

Strength of Recommendation: Weak, GRADE 2

References:

1. American Diabetes Association. Hyperglycemic crises in patients with diabetes mellitus. *Diabetes Care*. 2003;26(suppl 1):S109–S117.
2. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32(7):1335-1343.
3. De Beer K, Michael S, Thacker M, et al. Diabetic ketoacidosis and hyperglycaemic hyperosmolar syndrome – clinical guidelines. *Nurs Crit Care*. 2008;13(1):5-1.

PICO 10: *In adult ED patients with DKA and associated altered level of consciousness what are the indications/contraindications to intubation?*

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Population, Patient or Problem: Adults with DKA and altered level of consciousness

Intervention, Prognostic Factor, Exposure: Intubation

Comparison: Aggressive medical therapy and close monitoring

Outcome: impact on resolution of acidosis, aspiration pneumonia, time to DKA resolution, mortality

Design: RCTs or Systematic reviews.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: There is insufficient evidence to make DKA-specific recommendations regarding indications for intubation, however, case reports and experimental evidence in animals has shown that removing the patient's voluntary respiratory drive through paralysis or sedation, as well as the increased resistance to exhalation provided by the tube can lead to a precipitous rise in the PaCO₂ and an acute lowering of the patient's pH. If already significantly acidotic this can worsen patient outcomes.

Quality of Evidence: Very Low, GRADE D

Strength of Recommendation: Insufficient evidence

References:

1. Nunn JF. Control of breathing. In: Nunn JF. *Applied Respiratory Physiology*. 3rd ed.

London: Butterworths; 1987:72-79.

2. Marcin JP, Glaser N, Barnett P, et al. Factors associated with adverse outcomes in children with diabetic ketoacidosis-related cerebral edema. *J Pediatr*. 2002;141(6):793–797.
3. Tasker RC, Lutman D, Peters MJ. Hyperventilation in severe diabetic ketoacidosis. *Pediatr Crit Care Med*. 2005;6(4):405-411.

PICO 11: In adult ED patients with confirmed DKA is ICU admission required?

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Population, Patient or Problem: Adult ED patients with confirmed DKA

Intervention, Prognostic Factor, Exposure: ICU admission

Comparison: General ward admission

Outcome: morbidity, mortality, inpatient length of stay

Design: RCTs, Cohort studies or Systematic reviews.

Search Strategy: Cochrane library, Medline and PubMed for systematic reviews and clinical trials. Guidelines were searched.

Clinical Recommendation: There is insufficient evidence. To date only retrospective studies have addressed the indications for ICU admission. May et al developed a Severity of DKA grading system¹. Marinac in 2000 published a review of ICU appropriateness for DKA admissions where they determined that any patient who: met any one of the DKA severity III or IV criteria, which included serum bicarb less than or equal to 9, diastolic BP less than or equal to 60 mmHg, and serum osmolality greater than 330 OR had signs of mental obtundation or coma, additional medical conditions warranting ICU, shock or significant hypotension, hypothermia less than or equal to 35C, or age greater than 65 were considered appropriate ICU admissions². No systematic reviews or guidelines could be identified on whether admission to ICU is required for adult patients with DKA.

Quality of Evidence: Very Low, GRADE D

Strength of Recommendation: Insufficient evidence

References:

1. May ME, Young C, King J. Resource utilization in treatment of diabetic ketoacidosis in adults. *Am J Med Sci*. 1993;306(5):287-294.
2. Marinac JS, Mesa L. Using a severity of illness scoring system to assess intensive care unit admissions for diabetic ketoacidosis. *Crit Care Med*. 2000; 28(7):2238-2241.

Appendix B – PICO-D Methodology and GRADE Terminology

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Key components of high quality and trustworthy clinical guidance include: i) recommendations that are clearly stated and based on scientific evidence of benefits, harms and where possible, costs, and ii) a guideline rating system that is used to communicate quality and reliability of both the evidence and the strength of its recommendations. In the development of these guidelines, clinical questions were formulated based on the PICO-D format as supported by Sackett¹ and Guyatt² in their User's Guide to the Medical Literature to define the clinical question. The GRADE terminology, where possible, is used to address the questions regarding Quality of Evidence and Strength of Recommendations. The components of PICO-D format and the GRADE methodology are described below.

PICO-D

P - Population, Patient, or Problem: This element defines the group of patients or characteristics of the patients.

I - Intervention, Prognostic Factor, Exposure: This element defines the main intervention being considered.

C - Comparison: This element defines the main alternative to compare with the intervention, such as comparison of two drugs or tests, or a medication to no medication or placebo.

O - Outcome: This defines what you are trying to accomplish, measure, improve or affect.

D - Design: The type of question (related to diagnosis, harm/etiology, prognosis, or therapy) will define which study design is best suited to provide evidence to answer the clinical question.

Definitions of Study Types^{2,3}

1. **Meta-analysis:** a statistical technique that summarizes the results of several studies in a single weighted estimate, in which more weight is given to results of studies with more events and sometimes to studies of higher quality.
2. **Systematic Review:** attempts to collate all empirical evidence that fits pre-specified eligibility criteria to answer a specific research question using explicit, systematic methods selected with a view to minimizing bias. This provides more reliable findings from which to draw conclusions. (Antman 1992, Oxman 1993). The key characteristics of a systematic review are: i) clearly stated objectives with pre-defined eligibility criteria for studies; ii) an explicit and reproducible methodology; iii) a systematic search that attempts to identify all studies meeting the eligibility criteria; iv) an assessment of validity for the included studies, (e.g. through the assessment of risk of bias; and v) a systematic synthesis and presentation, of the characteristics and findings of the included studies.⁴
3. **Randomized Controlled Trial (RCTs):** a trial in which participants are randomly assigned to two or more groups: at least one (the experimental group) receiving an intervention that is being tested and another (the comparison or control group) receiving an alternative treatment or placebo. This design allows assessment of the relative effects of interventions.
4. **Controlled Clinical Trial (CCTs):** a trial in which participants are assigned to two or more different treatment groups in a non-randomized or quasi-randomized method. Examples of quasi-randomized allocation are birthdate and medical record numbers. Studies in which

the randomization process is not explicitly stated as randomized are considered CCTs. CCTs are more likely to suffer from bias than RCTs.

5. **Observational Studies:**

- a. **Cohort Study²:** an observational study in which a defined group of people (the cohort) is followed over time. The outcomes of people in subsets of this cohort are compared, to examine people who were exposed or not exposed (or exposed at different levels) to a particular intervention or other factor of interest. A prospective cohort study assembles participants and follows them into the future. A retrospective (or historical) cohort study identifies subjects from past records and follows them from the time of those records to the present.
- b. **Case control study:** a study design that examines a group of people who have experienced an event (usually an adverse event) and a group of people who have not experienced the same event, and looks at how exposure to suspect (usually noxious) agents differed between the two groups. This type of study design is most useful for trying to ascertain the cause of rare events, such as rare cancers.
- c. **Case Series:** analysis of series of people with the disease (there is no comparison group in case series).

GRADE Methodology

Whenever possible answers are identified from recent high quality guidelines or high quality systematic reviews and recommendations provided are based on GRADE definitions. Where guidelines or systematic reviews are not available to answer certain questions rapid reviews are undertaken and/or a consensus approach used to try to answer clinically relevant questions. **Only where the evidence is supportive and the benefits clearly outweigh the harm is a “we recommend” strength of recommendation applied.**

Table 1. GRADE Quality of Evidence²

High GRADE A	We have high confidence that the true effect lies close to that of the estimate of the effect.
Moderate GRADE B	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low GRADE C	Our confidence in the effect estimate is low: The true effect may be substantially different from the estimate of the effect.
Very low GRADE D	We have very low confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Table 2. GRADE Strength of Recommendations²

Strong GRADE 1	Strong recommendation, with desirable effects clearly outweighing undesirable effects/burdens (or vice versa). Wording of Recommendation: We recommend in favor of / We recommend against.....
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Weak GRADE 2	Weak recommendation, with desirable effects closely balanced with undesirable effects. Wording of Recommendation: We suggest in favor of / We suggest against
Insufficient evidence or no consensus	Wording of Recommendation: There is insufficient evidence or the confidence in the effect estimates is so low that the panel is unable to make a recommendation regarding....

References:

1. Sackett D, Richardson WS, Rosenburg W, Haynes RB. *How to practice and teach evidence based medicine*. 2nd ed. Churchill Livingstone; 1997.
2. Guyatt GH, Oxman AD, Vist GE, et al; for the GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008; 336(7650):924-926.
3. Clinical Questions, PICO & Study Designs: Formulating a Well Built Clinical Question. Dahlgren Memorial Library/ Georgetown University Medical Center. <http://researchguides.dml.georgetown.edu/ebmclinicalquestions>. Updated February 3, 2015. Accessed January 2015.
4. Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Appendix C – Patient Education and Discharge Materials

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Diabetic Ketoacidosis: After your visit

<https://myhealth.alberta.ca/health/AfterCareInformation/pages/conditions.aspx?hwId=tw12221>

Appendix D – Detailed Diabetic Ketoacidosis Emergency Department Visits

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Table 1. Diabetic Ketoacidosis Emergency Visits 2012 – 2014^a

Zone	Facility	Year	ED Visits	# Admits	% Admits	# by EMS	% by EMS	# Transfer to Another Acute Site	% Transfer to Another Acute Site	
Calgary	Foothills Medical Centre	2012	68	64	94.1%	46	67.6%	0	0.0%	
		2013	85	81	95.3%	48	56.5%	0	0.0%	
		2014	82	80	97.6%	43	52.4%	0	0.0%	
	Peter Lougheed Centre	2012	100	90	90.0%	42	42.0%	0	0.0%	
		2013	86	74	86.0%	38	44.2%	0	0.0%	
		2014	53	48	90.6%	23	43.4%	1	1.9%	
	Rockyview General Hospital	2012	89	79	88.8%	44	49.4%	0	0.0%	
		2013	73	65	89.0%	47	64.4%	1	1.4%	
		2014	69	58	84.1%	40	58.0%	1	1.4%	
	South Health Campus	2013	36	34	94.4%	17	47.2%	1	2.8%	
		2014	44	39	88.6%	24	54.5%	0	0.0%	
		Total		785	712	90.7%	412	52.5%	4	0.5%
	Central	Red Deer Regional Hospital Centre	2012	37	27	73.0%	19	51.4%	0	0.0%
			2013	46	34	73.9%	24	52.2%	0	0.0%
2014			64	52	81.3%	28	43.8%	1	1.6%	
	Total		147	113	76.9%	71	48.3%	1	0.7%	
Edmonton	Grey Nuns Community Hospital	2012	22	16	72.7%	6	27.3%	0	0.0%	
		2013	39	34	87.2%	13	33.3%	0	0.0%	
		2014	31	19	61.3%	11	35.5%	0	0.0%	
	Misericordia Community Hospital	2012	50	43	86.0%	25	50.0%	0	0.0%	
		2013	42	38	90.5%	13	31.0%	0	0.0%	
		2014	48	41	85.4%	13	27.1%	0	0.0%	
	Northeast Community Health Centre	2012	7	0	0.0%	1	14.3%	5	71.4%	
		2013	7	0	0.0%	0	0.0%	6	85.7%	
		2014	6	0	0.0%	0	0.0%	4	66.7%	
	Royal Alexandra Hospital	2012	40	36	90.0%	28	70.0%	0	0.0%	
		2013	69	64	92.8%	47	68.1%	0	0.0%	
		2014	50	47	94.0%	41	82.0%	0	0.0%	
	Sturgeon Community Hospital	2012	29	26	89.7%	12	41.4%	1	3.4%	
		2013	24	22	91.7%	8	33.3%	0	0.0%	
		2014	32	32	100.0%	16	50.0%	0	0.0%	
	University of Alberta Hospital	2012	55	49	89.1%	30	54.5%	1	1.8%	
		2013	75	65	86.7%	36	48.0%	0	0.0%	
		2014	72	55	76.4%	33	45.8%	0	0.0%	
	Total		698	587	84.1%	333	47.7%	17	2.4%	
North	Northern Lights Regional Health Centre	2012	18	16	88.9%	6	33.3%	0	0.0%	
		2013	26	23	88.5%	6	23.1%	0	0.0%	
		2014	32	28	87.5%	11	34.4%	0	0.0%	
	Queen Elizabeth II Hospital	2012	29	24	82.8%	8	27.6%	0	0.0%	
		2013	23	17	73.9%	7	30.4%	0	0.0%	
		2014	28	22	78.6%	13	46.4%	0	0.0%	
	Total		156	130	83.3%	51	32.7%	0	0.0%	
South	Chinook Regional Hospital	2012	16	15	93.8%	2	12.5%	0	0.0%	
		2013	28	26	92.9%	10	35.7%	0	0.0%	
		2014	27	24	88.9%	11	40.7%	0	0.0%	
	Medicine Hat Regional Hospital	2012	14	13	92.9%	5	35.7%	0	0.0%	
		2013	19	18	94.7%	8	42.1%	0	0.0%	
		2014	21	20	95.2%	8	38.1%	0	0.0%	
		Total		125	116	92.8%	44	35.2%	0	0.0%
	Grand Total		1911	1658	86.8%	911	47.7%	22	1.2%	

^aData provided by AHS Data Integration, Management and Reporting (DIMR)¹

References: Data provided by AHS Data Integration, Management and Reporting (DIMR). February 2015.

Appendix E – Clinical Working Group Membership

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We would like to acknowledge the contributions of the Provincial Clinical Knowledge Working Group members as follows. Your participation and time spent is appreciated

Emergency Department Diabetic Ketoacidosis Knowledge Topic Working Group Membership

Name	Title	Role	Zone
<i>Knowledge Lead</i>			
Michael Bullard	Physician	Knowledge Lead	Provincial
<i>Topic Lead</i>			
Lyle Thomas	Physician	Topic Lead	Provincial
<i>Working Group Members</i>			
Harvey Woytiuk	Physician	Working Group Member	North Zone
Richard Martin	Physician	Working Group Member	North Zone
Pat San Augustin	Physician	Working Group Member	North Zone
Brian Holroyd	Physician	Working Group Member	Edmonton Zone
Jennifer Pritchard	Physician	Working Group Member	Edmonton Zone
Sam Chow	Physician	Working Group Member	Edmonton Zone
Ni Lam	Physician	Working Group Member	Edmonton Zone
Ali Kirkham	Physician	Working Group Member	Edmonton Zone
Katherine Smith	Physician	Working Group Member	Edmonton Zone
Simon Ward	Physician	Working Group Member	Central Zone
Lyle Thomas	Physician	Working Group Member	Central Zone
Eddy Lang	Physician	Working Group Member	Calgary Zone
Shawn Dowling	Physician	Working Group Member	Calgary Zone
Chris Hall	Physician	Working Group Member	Calgary Zone
Andrew McRae	Physician	Working Group Member	Calgary Zone
Paul Parks	Physician	Working Group Member	South Zone
Dan Banmann	Physician	Working Group Member	South Zone
Jennine Desmarais	Registered Nurse	Working Group Member	North Zone
Shelly Lynn Franklin	Registered Nurse	Working Group Member	North Zone
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Maria Janik	Registered Nurse	Working Group Member	Edmonton Zone
Laura Fowler	Registered Nurse	Working Group Member	Central Zone
Thora Skeldon	Registered Nurse	Working Group Member	Central Zone
Aaron Shaw	Registered Nurse	Working Group Member	Calgary Zone
Bonnie Niebergall	Registered Nurse	Working Group Member	South Zone
Monique Fernquist	Registered Nurse	Working Group Member	Provincial
<i>Multidisciplinary</i>			
Colin MacDonald	Physician	Content Expert	Edmonton Zone
Stafford Dean	DIMR Representative	Content Expert	Provincial
Bill Anderson	Physician - DI	Content Expert	Provincial
James Wesenberg	Physician – Laboratory Med	Content Expert	Provincial
Steve Freriks	Pharmacy Representative	Content Expert	Provincial

Nicholas Myers	Physician	Primary Care Representative	Calgary Zone
Rod Elford	Physician	Primary Care Representative	Calgary Zone
Sophia Christoforakis	SCN Representative	Surveyor	Provincial

Thank you to the following clinicians who participated in the colleague review process. Your time spent reviewing the knowledge topics and providing valuable feedback is appreciated: Yang Li, Nadder Sharif, Shazma Mithani, Don Nixon, Bill Hendriks, Patrick Linehan, James Reid, Jennifer Shiu, Duane Bates, Scott Ross

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