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Are the results from the 2014 UK national survey on the management of diabetic ketoacidosis applicable to individual centres?

M. Varadarajan, M. Patel, N. Kakkar, E. Li Ping Wah-Pun Sin, D. Maxey, I. Nunney, K. Dhatariya

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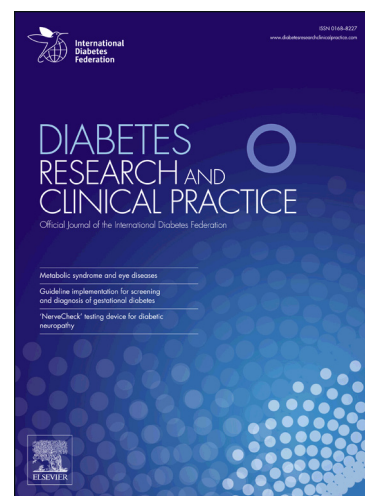
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**Title:**

Are the results from the 2014 UK national survey on the management of diabetic ketoacidosis applicable to individual centres?

**Authors:**

M Varadarajan<sup>1</sup>

M Patel<sup>1</sup>

N Kakkar<sup>1</sup>

E Li Ping Wah-Pun Sin<sup>1</sup>

D Maxey<sup>1</sup>

I Nunney<sup>1</sup>

K Dhatariya<sup>1,2</sup>

**Affiliations**

1. Norwich Medical School, University of East Anglia, Norwich, Norfolk, NR4 7TJ
2. Norfolk and Norwich University Hospitals NHS Foundation Trust, Colney Lane, Norfolk, NR4 7UY

**Corresponding author:**

Dr Ketan Dhatariya

Consultant in Diabetes and Endocrinology,

Elsie Bertram Diabetes Centre,

Norfolk and Norwich University Hospitals NHS Foundation Trust,

Colney Lane,

Norwich, Norfolk, UK

NR4 7UY

Tel: +44 (0)1603 288170

Fax: +44 (0)1603 287320

Email: ketan.dhatariya@nnuh.nhs.uk

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## **Abstract**

### **Background**

In 2013 the Joint British Diabetes Societies published an update to their 2010 guideline on the management of diabetic ketoacidosis (DKA). In 2014 a national survey was conducted to assess the management of DKA across the UK using the JBDS or local guidelines. Hospitals were invited to submit data on 5 people presenting with DKA. These data were published in 2016. However, whether those national results were applicable to individual hospitals remains unknown.

### **Aim**

To assess the management of people presenting with DKA at a single hospital and compare the results with the national dataset.

### **Methods**

Using the identical data collection tool as used in the national survey we collected information on 40 subjects (a total of 52 admissions) admitted with DKA between April 2014 and July 2015.

### **Results**

The data collected locally were very similar to those found in the national dataset. The management of DKA was best during the first few hours after admission, then biochemical and physical monitoring frequency decreased. The number of people who developed hypokalaemia and hypoglycaemia were very similar to the national data. Rates of biochemical improvement were slightly better locally.

### **Conclusions**

The data from the national DKA survey, even though based on a maximum of 5 people per hospital from across the UK are applicable at a hospital level.

## **Introduction**

Diabetic ketoacidosis (DKA) is a potentially life-threatening metabolic complication predominantly affecting people with type 1 diabetes. It usually requires hospital admission, and has an appreciable mortality rate [1]. In an attempt to standardise the management of DKA, in 2010 the Joint British Diabetes Societies (JBDS) produced a guideline that has been widely used [2]. These nationally accepted guidelines standardised the criteria for the diagnosis of DKA as a blood glucose concentration of  $>11.0$  mmol/L or a known diagnosis of diabetes mellitus; a pH of  $<7.3$ ; and significant ketonuria ( $>2+$ ) or ketonaemia  $>3.0$ mmol/L. They were updated in 2013 [3], and this update formed the basis of a national survey carried out in 2014 [4,5].

The national DKA survey reported the results from 72 UK hospitals assessing their adherence to the JBDS (or local) guidelines in the management of up to 5 consecutive patients presenting to their institution. Initial monitoring and management with adequate fluid resuscitation and use of weight-based fixed-rate intravenous insulin infusion was found to be excellent [4]. However, the quality of subsequent care was found to be suboptimal, with significant numbers of patients experiencing hypokalaemia and hypoglycaemia (55% and 27.6% respectively). However, these data are from a small number of individuals at any one hospital and what remains uncertain is if the results of the national survey are applicable to a single institution. Thus, the current study was carried out to assess the generalisability and reliability of the national survey results to a single institute.

### **Patients and methods**

We performed a retrospective analysis of patients presenting to our hospital with a confirmed diagnosis of DKA between April 2014 and July 2015. The aim was to compare our local data to that published in the national survey. Patients were found using the hospital Patient Administration System, or using the electronic discharge summaries, and also using the records of the diabetes inpatient specialist nurse records. They would see all patients admitted with DKA under the Best Practice Tariff arrangement [6].

To allow direct comparison of outcomes, the data collection questionnaire utilised in the national survey was also used in this audit (Appendix 1). This questionnaire was based on the JBDS guideline and collated information on the management of DKA from the time of admission to post-discharge. This also included data on biochemical and clinical monitoring, as well as those on the adherence to the national guidelines. All patient data were obtained by five of the authors. Data were anonymised and stored in password protected files and were analysed using SPSS software (IBM Ltd, Portsmouth, UK).

The survey was registered with the Clinical Audit and Improvement Department of the NNUH NHS Foundation Trust. No ethical approval was required because this was deemed to be a service improvement exercise.

## **Results**

40 patients were assessed, with a total of 52 admissions. The demographics of the patients are compared in Table 1.

There was a greater female preponderance in the local data, and a majority of people classified as 'White' ethnicity.

### *Management in the first hour (Table 2)*

Locally, 100% of DKA diagnoses were made in accordance with the JBDS guidelines, compared to only 71.4% nationally. In addition, all patients locally were seen by a senior trainee or consultant. More people locally were given a 'stat' insulin dose compared to national data and fewer people received the recommended initial fluid replacement of choice. The majority of the other measured parameters were in line with national data. However, three other variables had marked differences. Foot examination was performed much more frequently in patients locally compared to nationally (71.2% vs 33.9% respectively). However, urea and electrolyte concentrations (78.8% vs 98.9%) and chest X-ray (42.3% vs 69.3%) were performed much less frequently locally than nationally.

### *Biochemical changes in first 24 hours (Figures 1a – 1c)*

These were very broadly similar between the local and national data. Admission mean pH ( $\pm$ SD) was 7.15( $\pm$ 0.17) locally, and 7.16 ( $\pm$ 0.15) nationally, the mean glucose was 29.4 mmol/l ( $\pm$ 19.0) locally and 28.7 mmol/l ( $\pm$ 10.9) nationally. Mean

blood ketone concentration was 5.06 mmol/l ( $\pm 1.6$ ) locally, 5.68 mmol/l ( $\pm 1.5$ ) nationally. Mean bicarbonate was 13.3 mmol/l ( $\pm 6.2$ ) locally, and 11.3 mmol/l ( $\pm 5.1$ ) nationally. The mean potassium on admission was 5.0 mmol/l ( $\pm 1.2$ ) locally and 4.8 mmol/l ( $\pm 1.0$ ) nationally. Figures 1a, 1b and 1c show the changes in potassium, pH, and bicarbonate concentrations during the course of the 24 hours following admission showing very similar rates of change between the local and national data.

#### *Adherence to guidelines (Table 3)*

The management of patients after the initial hour to 24 hours is shown in Table 3. 23.1% of patients did not have potassium replaced as per local guidelines. This finding is similar to the national findings in which 20.1% of respondents felt that potassium replacement was not carried out in accordance with their guidelines. This also reflects in the percentage of patients whose potassium levels remained in the reference ranges (local - 44.2%, national - 43.1%). However, fixed rate intravenous insulin infusions were given appropriately with accordance to the guidelines more frequently locally (98.1%), than nationally (90.5%). In addition, more people locally (88.5%) had an appropriate established monitoring regimen than nationally (70.3%).

Fewer patients locally developed hypoglycaemia - 13.5% vs 27.6% nationally. The other major difference was the percentage of patients reviewed by a senior if progress was unsatisfactory (locally 90.4% vs nationally 33.2%).

*Resolution and on-going in-hospital management (Table 4)*

Figure 1 shows the rate of biochemical resolution was slightly faster locally, with the mean pH reaching 7.3 at 6 hours (just over 7 hours nationally), and the mean bicarbonate concentration reaching 15.0mmol/l at 4 hours (just under 6 hours nationally). The rates of DKA resolution were similar between the two groups. However, locally there was much greater monitoring and involvement of senior medical staff and the specialist diabetes team during the acute phase of the illness than nationally, although after resolution, the rates of diabetes team involvement was almost identical.

*Discharge planning (Table 5)*

Table 5 shows the steps involved prior to discharge.

**Discussion**

This single centre study shows that data from the national survey on the management of DKA are applicable to our – and probably other – individual sites.

The original national survey was undertaken to assess the management of DKA across the UK [4]. However, by using a very few number of individuals from any one institution, there was a risk that when pooled, the data would be nationally representative, but may not have been applicable to an individual site. In addition, whilst the original survey had asked for consecutive admissions to be included, there was the risk of selection bias from sites when choosing whose data to submit.



A previous single centre study had been conducted looking at outcomes using the first version of the DKA guideline [7]. They also looked at 50 cases of people with a discharge code of DKA admitted between February and December 2012. They found that 46% of their cohort developed hypokalaemia and that 70% had not had their potassium replaced according to the guidelines. In addition, they also found that 40% of their cohort experienced hypoglycaemia, with 20% of people not having 10% dextrose prescribed correctly [7]. Overall, they found that, as with this study and the national survey, the initial management during the first hour after admission management was very good. However, it was in the subsequent time that the guidelines were not followed as vigorously, with metabolic monitoring, fluid balance and hypoglycaemia being areas for concern [4,7]. The authors of that study, and the national survey found that diabetes specialist team involvement was high once the immediate management period had passed.

There were, however, several issues with the previous local audit that the authors themselves acknowledged. They had 172 admissions with DKA, and they chose to look at 100 of those. However, they were unable to include several of those into their dataset because they had not used the correct prescription chart or proforma, others had been admitted directly to the intensive care unit, and several others were coded as having DKA but on closer inspection, had other diagnoses. The strength of the current study is that we had a consecutive cohort of admissions with a full dataset on everyone, with no selection bias.

Another strength of the current study is that it looked at the most up to date version (2013) of the DKA guideline. Furthermore, the current study used the same data collection tool that was used in the national survey allowing for a direct comparison to be made, and there were many fewer missing data.

During treatment 51.9% of patients locally developed hypokalaemia and 13.5% developed hypoglycaemia. These findings are similar to those found in the national survey. However, it is unknown as to whether the guidelines were used when caring for those who developed hypokalaemia or hypoglycaemia and those who did not. It may well be that to prevent these, the rate of insulin infusion should be halved when the glucose or ketone concentrations fall, to reduce the rate of intracellular potassium uptake.

A limitation that must be acknowledged is that the lead author of the national guideline works at our hospital. It is possible that his presence there influenced the junior medical staff at the front door who manage the patients admitted with DKA for the first few hours. In addition, several of the senior medical staff in the acute medical unit are also trained in diabetes and endocrinology, thus prone to ensure greater adherence to the national guideline. This is also likely to have been a factor as to why a higher proportion of patients were reviewed by a senior member of staff, particularly when metabolic improvement was not being seen.

The process and completion of the discharge were also examined. There were more people with diabetes receiving psychological support before being discharged in the local study (65% more patients received support). At the time of the data collection

our service had ready access to psychological services, something that has been advocated for people with DKA [6]. However soon after the study ended, funding for this service was withdrawn. The percentage of correct insulin doses written was also higher locally compared to the national study. However, fewer discharge letters contained the correct information. In the questionnaire used for this study, other questions about discharge were also addressed such as the name of insulin, follow-up appointments and GP's receiving care plans. The results showed room for improvement across all the discharge fields. Our local data also showed several areas that needed improvement. These included that only 40% of people were followed up within 30 days; only 7% of discharge plans were sent to the GP; 23% of patients did not have ketone testing on discharge; 71.2% of patients did not have any written care plan with the diabetes inpatient specialist team; and that 10% of patients developed post-discharge complications. These results, in line with the national data, suggest that more communication between the patient and the specialist team, and between secondary and primary care may need to occur and that discharge summaries need to be improved.

In summary, our data have shown that the management of DKA locally was very similar to that seen in the 2014 national DKA survey. There remain areas of good practice, especially in the first few hours, but that a significant proportion of people develop hypokalaemia and hypoglycaemia. These data once again suggest that either the guidelines need to be better followed, or that the rate of insulin infusion needs to be changed once glucose or ketone concentrations fall. Further work needs to be done to decide what the best course of action should be.

Permissions:

Permission has been granted by John Wiley and Sons to reproduce the data in the tables and figures from Reference [4].

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## Legends

### Table 1

Baseline demographics of patients. National data are taken from reference [4]

### Table 2

Management of the patient in the first hour after diagnosis of DKA was made. The number and percentage of missing data for each variable is shown. National data are taken from reference [4]

JBDS – Joint British Diabetes Societies for Inpatient Care Group

ICU – Intensive Care Unit

FRIII – Fixed Rate Intravenous Insulin Infusion

ECG – Electrocardiogram

CXR – Chest X-Ray

### Table 3

Ongoing management between 1 and 24 hours after the diagnosis of DKA was made.

National data are taken from reference [4]

FRIII – Fixed Rate Intravenous Insulin Infusion

EWS – Early Warning Score

## References

- [1] Health and Social Care Information Centre. National Diabetes Inpatient Audit (NaDIA) - 2015. <http://www.hscic.gov.uk/catalogue/PUB20206> . 2016.
- [2] Savage MW, Dhatariya KK, Kilvert A *et al.* Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. *Diabetic Med* 2011; **28**(5):508-515.
- [3] Dhatariya K, Savage M, Claydon A *et al.* Joint British Diabetes Societies Inpatient Care Group. The management of diabetic ketoacidosis in adults. Second Edition. Update: September 2013. [http://www.diabetologists-abcd.org.uk/JBDS/JBDS IP DKA Adults Revised.pdf](http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_DKA_Adults_Revised.pdf) . 2013.
- [4] Dhatariya KK, Nunney I, Higgins K, Sampson MJ, Iceton G. A national survey of the management of diabetic ketoacidosis in the UK in 2014. *Diabetic Med* 2016; **33**(2):252-260.
- [5] Dhatariya K, Nunney I, Iceton G. Institutional factors in the management of adults with diabetic ketoacidosis in the UK: results of a national survey. *Diabetic Med* 2016; **33**(2):269-270.
- [6] Price H, Thomsett K, Newton I, Alderson S, Hillson R. Developing best practice tariffs for diabetic ketoacidosis and hypoglycaemia. *Pract Diab* 2013; **30**(1):6-8.
- [7] Crasto W, Htike ZZ, Turner L, Higgins K. Management of DKA following implementation of the JBDS DKA guidelines: Where we are and where should we go? *Br J Diabetes Vasc Dis* 2015; **15**(1):11-16.

**Table 4**

Data showing the management of DKA beyond 24 hours, once the resolution of DKA had been confirmed. National data are taken from reference [4]

s.c. – subcutaneous

**Table 5**

Data showing the management of DKA once resolution had been confirmed. National data are taken from reference [4]

GP – General Practitioner

**Figure 1a**

Potassium concentrations in people presenting with DKA - National vs Local. The error bars are  $\pm 1SD$

**Figure 1b**

pH Values in people presenting with DKA - National vs Local. The error bars are  $\pm 1SD$

**Figure 1c**

Bicarbonate concentration in people presenting with DKA - National vs Local. The error bars are  $\pm 1SD$

**Online Appendix 1**

Questionnaire used in the data collection

Table 1 – Baseline Demographics.

	NNUH	National
<b>Gender %</b>		
Male	32.7	51.9
Female	67.3	46.3
Missing data	0	1.8
<b>Ethnicity, %</b>		
White	88.5	81.6
Mixed white/ Asian or white /black	5.8	0.8
Indian/Asian	0	1.4
African /black	1.9	1.5
Other	2.8	0.4
Missing data	1	14.5



Table 2

Variable	NNUH			National		
	Yes %	No %	Missing data n (%)	Yes (%)	No (%)	Missing data n (%)
Was the Diagnosis Made Using JBDS Criteria?	100	0	0	71.4	18.7	28 (9.9)
Seen by ICU or a Senior?	100	0	0	85.9	7.1	19 (6.7)
Was a 'Stat' Insulin Dose Given?	48.1	51.9	0	14.8	84.1	3 (1.1)
Was 0.9% Sodium Chloride Solution Used?	86.5	13.5	0	96.5	3.2	1 (0.4)
Was an FRIII used?	90.4	9.6	0	91.5	8.5	0 (0)
Potassium Replacement in Accordance with Local Protocol?	80.8	19.2	0	79.9	12.9	20 (7.2)
Early Warning Score Recorded?	94.2	3.8	1.9	91.2	3.2	16 (5.7)
Respiratory Rate Recorded?	98.1	1.9	0	96.5	0.4	9 (3.2)
Temperature Recorded?	100	0	0	95.4	0	13 (4.6)
Pulse Rate Recorded?	100	0	0	97.2	0	8 (2.8)
Oxygen Saturations Recorded?	100	0	0	97.2	0	8 (2.8)
Glasgow Coma Scale	82.7	15.4	1.9	89.8	6.7	10 (3.5)

Recorded?						
Full History Recorded?	92.3	7.7	0	95.8	3.2	3 (1.1)
Full Examination Recorded?	92.3	7.7	0	92.6	3.2	11 (3.9)
Foot Examination Recorded?	71.2	25	3.8	33.9	47.7	52 (18.4)
Blood Ketones Recorded?	90.4	9.6	0	80.9	15.9	9 (3.2)
Capillary Blood Glucose Recorded?	90.4	9.6	0	97.5	0.7	5 (1.8)
Venous Plasma Glucose Recorded?	94.2	5.8	0	93.3	4.2	7 (2.5)
Urea and Electrolytes Recorded?	78.8	17.3	3.8	98.9	0	3 (1.1)
Venous Blood Gases Recorded?	94.2	5.8	0	92.9	5.7	4 (1.4)
Full Blood Count Performed?	82.7	13.5	3.8	92.2	3.2	13 (4.6)
ECG Performed?	73.1	23.1	3.8	79.9	14.1	17 (6.0)
CXR Performed?	42.3	50	7.7	69.3	23.7	20 (7.1)
Urinalysis Performed?	59.6	30.8	9.6	74.9	13.1	34 (12)

Table 3

Variable	NNUH			National		
	Yes %	No %	Missing data n (%)	Yes (%)	No (%)	Missing data n (%)
Was IV 0.9% Sodium Chloride Solution Replacement Given as per Local Guidance?	90.4	9.6	0	89.4	9.9	2 (0.7)
Was a FRIII used as per Local Guidance	98.1	1.9	0	90.5	7.8	5 (1.8)
Capillary Glucose Levels Measured Hourly?	88.5	11.5	0	81.6	13.1	15 (5.3)
Observations of Vital Signs taken Hourly?	82.7	17.3	0	67.8	26.9	15 (5.3)
EWS measured Hourly?	82.7	17.3	0	67.1	32.5	21 (7.4)
Urine Output Documented?	78.8	19.2	1.9	74.2	22.6	9 (3.2)
Was 10% Glucose started when the Glucose Dropped to <14mmol/l?	63.5	32.7	3.8	82.7	15.2	6 (2.1)
Review of Fluid Balance with the Rate of Normal Saline Amended if Appropriate?	94.2	5.8	0	68.9	20.8	29 (10.2)
Was a Long Acting Insulin Continued?	63.5	25	11.5	58.3	38.5	8 (2.8)
Was there a Review of	86.5	13.5	0	85.9	5.7	22 (7.8)

Metabolic Response to Treatment?						
If Yes, Were Appropriate Changes in Treatment Made?	88.5	3.8	7.7	58.7	10.2	86 (30.4)
Was a Precipitating Cause Found?	80.8	19.2	0	77.0	13.8	25 (8.8)
Was a Referral to Diabetes Team Made?	98.1	1.9	0	92.6	4.2	9 (3.2)

Table 4

Variable	NNUH			National		
	Yes %	No %	Missing data n (%)	Yes (%)	No (%)	Missing data n (%)
Was resolution of DKA confirmed?	78.8	17.3	3.8	83.1	9.2	22 (7.8)
Treatment and monitoring reviewed by specialist registrar /consultant on-call?	31.7	48.1	19.2	11.0	67.5	61 (21.6)
Was the specialist diabetes team involved during the acute phase?	100	0	0	13.4	53.0	95 (33.6)
Was this transition to s.c. insulin managed appropriately?	86.5	3.8	9.6	83.4	12.4	12 (4.2)
After DKA resolution was the patient reviewed by the Diabetes Inpatient Specialist Team?	94.2	1.9	3.8	95.1	3.9	3 (1.1)

Table 5

Variable	NNUH			National		
	Yes %	No %	Missing data n (%)	Yes (%)	No (%)	Missing data n (%)
Did the patient receive education support before discharge?	86.5	11.5	1.9	86.8	8.8	13 (4.6)
Did the patient receive psychological support before discharge?	73.1	23.1	3.8	82.7	8.1	26 (9.2)
Did the discharge letter contain all the correct clinical information?	80.8	15.4	3.8	91.2	2.5	17 (6.0)
Did the discharge letter contain the correct insulin dose?	88.5	5.8	5.8	76.3	15.5	23 (8.1)
Did the discharge letter contain the correct delivery device?	69.2	19.2	11.5	56.9	32.5	30 (10.6)
Did the discharge letter contain the correct insulin name?	40.4	30.8	28.8	83.7	8.8	20 (7.1)
Did follow-up by Diabetes Inpatient Specialist Team	40.4	30.8	28.8	54.1	31.1	41 (14.5)

take place within 30 days?						
Were there any post-discharge complications	9.3	79.2	11.5	9.2	83.0	22 (7.8)
Was there a written care plan between patient and Diabetes Inpatient Specialist Team?	15.4	71.2	13.4	46.6	41.3	34 (12.0)
Was a copy of the care plan sent to GP?	6.8	87.5	5.7	53.4	38.2	24 (8.5)
Did the patient have access to ketone testing on discharge?	54.5	22.9	22.6	55.5	26.1	52 (18.4)

Figure 1a

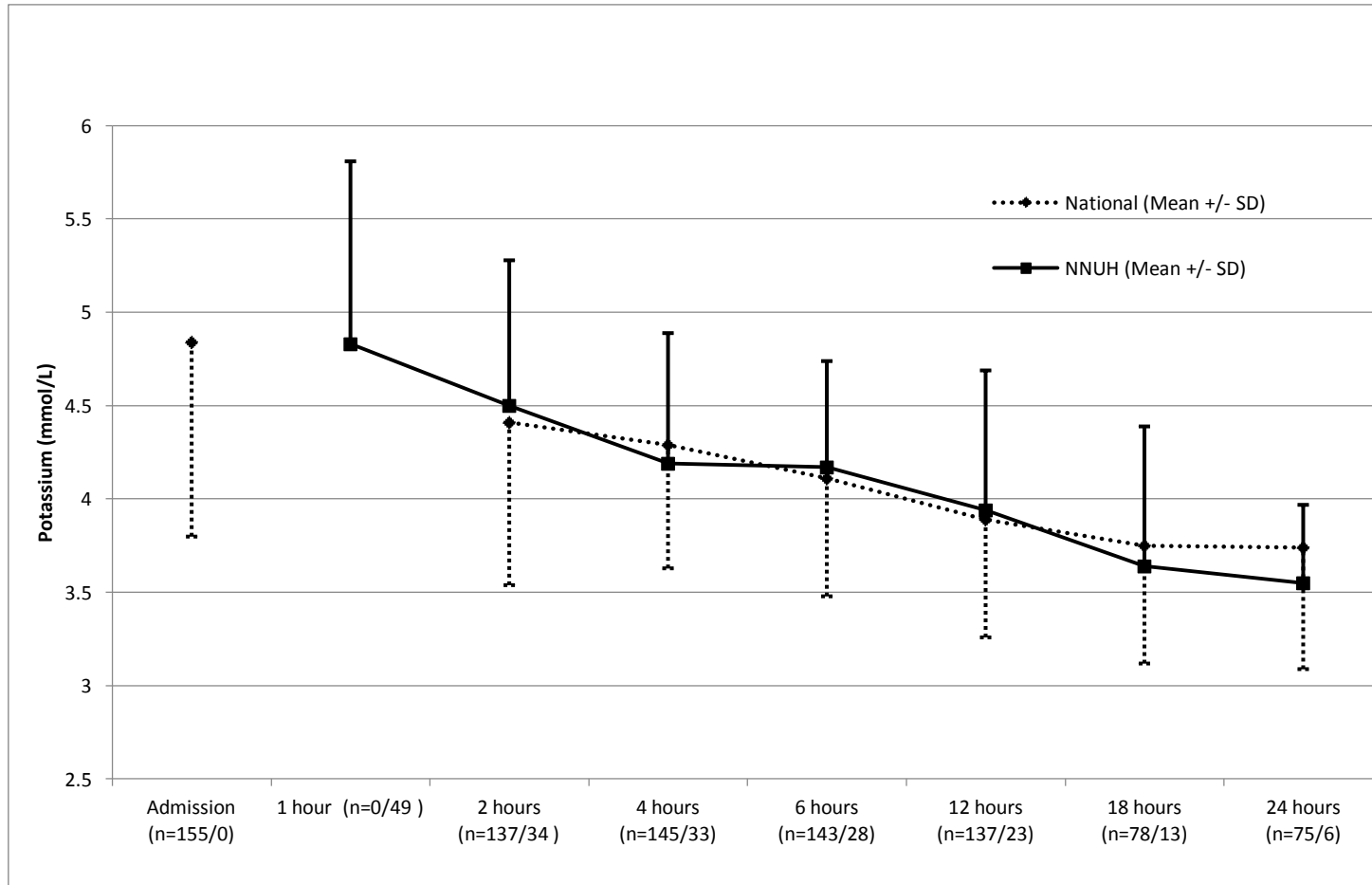




Figure 1b

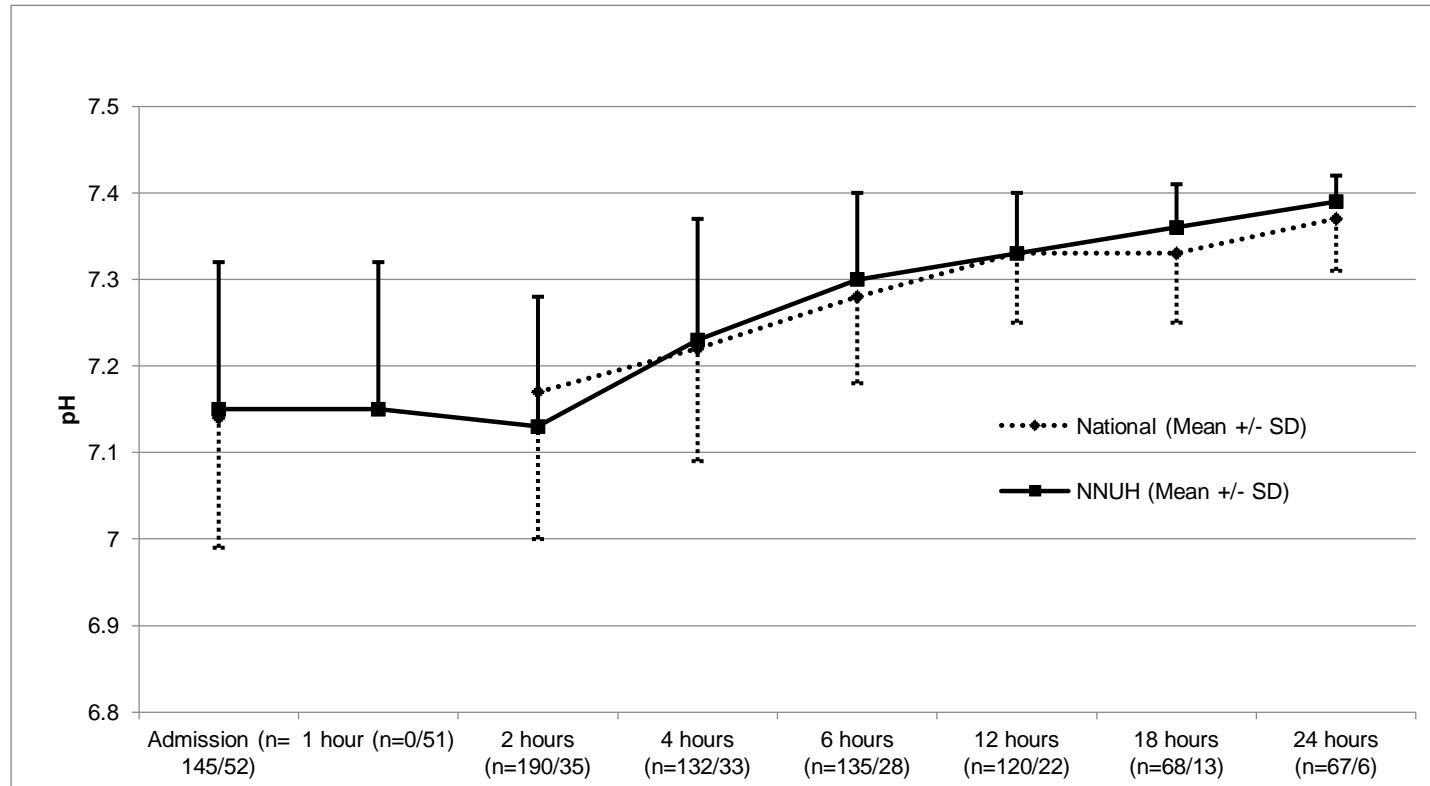
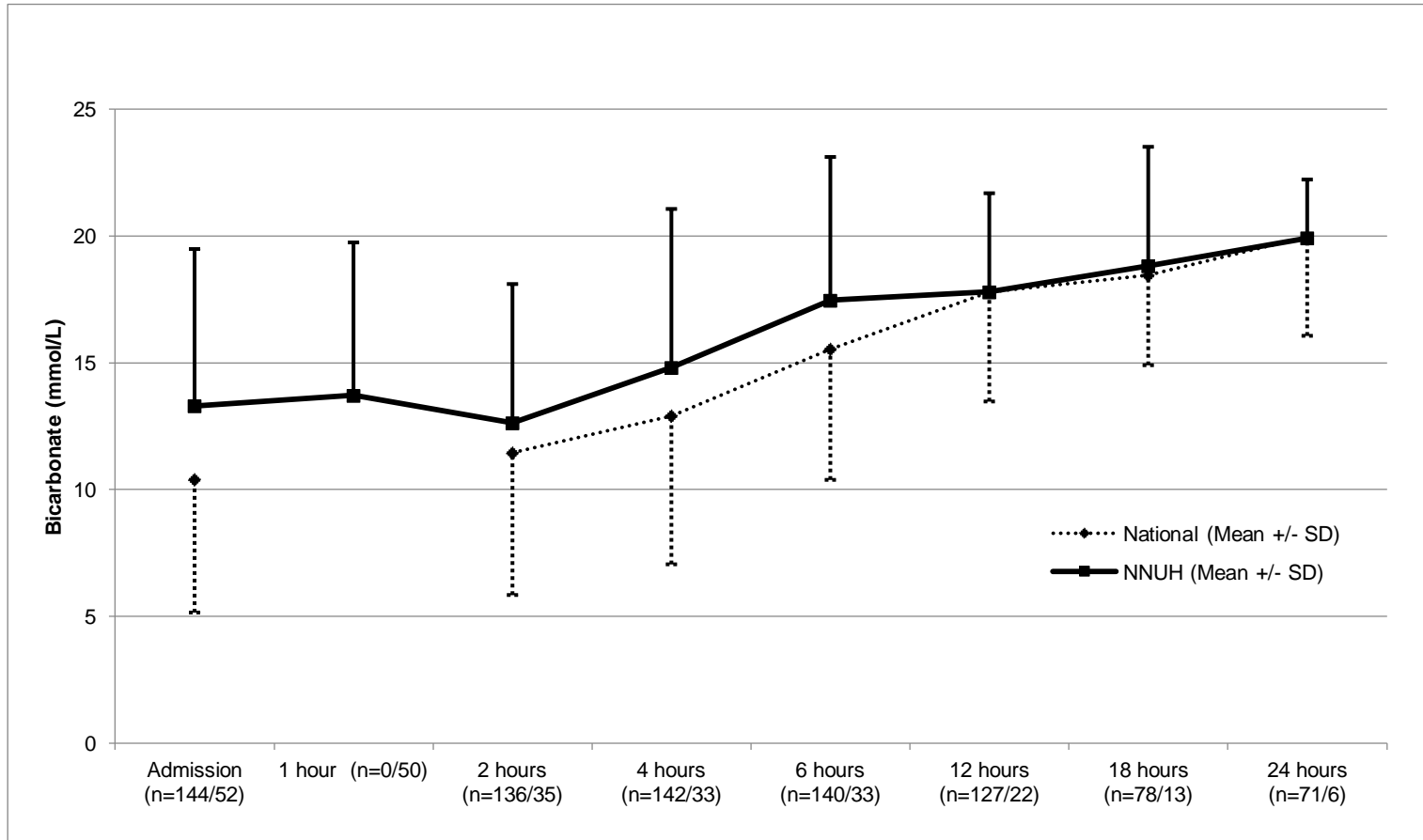


Figure 1c



**Highlights**

Data from a large national survey on the management of diabetic ketoacidosis (DKA) looked at outcomes of up to 5 people presenting to a single institution. However, whether these national data are applicable to individual hospitals is unknown

Our data are very similar to the national dataset, showing that the management of DKA was best in the first hour and then guidelines were adhered to less often after that.

Work needs to be done to improve adherence to guidelines, and a discussion is necessary as to whether the rate of intravenous insulin should be reduced when glucose concentrations drop.