## **Research: Care Delivery**

# Diabetic ketoacidosis in an adolescent and young adult population in the UK in 2014: a national survey comparison of management in paediatric and adult settings

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## Abstract

**Aims** To assess the management of diabetic ketoacidosis in young people, which differs in the UK between paediatric and adult services, and to evaluate outcomes and extent to which national guidelines are used.

**Methods** A standardized questionnaire was sent to all paediatric and adult diabetes services in England, requesting details of all diabetic ketoacidosis admissions in young people aged > 14 years in paediatric services ('paediatric' patients), and in young adults up to the age of 22 years in adult services ('adult' patients).

**Results** A total of 64 adult patients aged  $\leq 22$  years (mean age 19.2 years) were reported, of whom seven were aged between 10 and 16 years. A total of 71 paediatric patients were reported [mean (range) age 14.9 (11–18) years]. We found that 85% of paediatric and 69% of adult patients were treated according to national guidelines, 99% of paediatric and 89% of adult patients were treated with 0.9% saline and fixed-rate insulin infusions and 16% of adult patients received an insulin bolus. Insulin treatment was initiated later in paediatric patients than in adult patients (100 vs 39 min; P < 0.001). In 23% of adult patients and 8.8% of paediatric patients, potassium levels were < 3.5 mmol/l (P < 0.005). The lowest mean potassium levels were 3.8 mmol/l in paediatric and 3.5 mmol/l in adult patients (P < 0.005). Hypoglycaemia occurred in 42.3% of paediatric and 36% of adult patients. Time to resolution was similar in paediatric and adult patients (16.0 vs 18.2 h), as was duration of hospital stay (2.35 vs 2.53 days).

**Conclusions** Young people were treated according to national guidelines, but the quality of monitoring was variable in both paediatric and adult settings. The incidence of hypoglycaemia and hypokalaemia was unacceptably high.

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## Introduction

Diabetic ketoacidosis, is a common cause of hospital admission and a significant contributor to mortality and morbidity in people with Type 1 diabetes [1,2]. Guidelines for the management of diabetic ketoacidosis in children have been available in the UK through the British Society of Paediatric Endocrinology and Diabetes (BSPED) since 1994 and are now widely used in paediatric departments [3]. Management guidelines have developed over the last 20 years to take into account emerging evidence for the prevention of cerebral oedema, which is the most serious complication of diabetic ketoacidosis in children and young people [4]. This includes reduced fluid volumes, delay in starting insulin infusion and emphasis on close monitoring [5–7].

The management of diabetic ketoacidosis in adults has historically involved giving significantly larger amounts of fluid in rehydration, and the use of variable insulin doses. In 2010 the UK Joint British Diabetes Societies (JBDS) published national guidance on the management of diabetic ketoacidosis [8,9], and revised this in 2013 [10]. These guidelines have become more similar to paediatric guidelines, in that recommended fluid volumes have been reduced, and a weight-based, fixed-rate intravenous insulin infusion is

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## What's new?

- Teenagers and young adults with diabetic ketoacidosis are treated largely according to national guidelines.
- Monitoring during treatment is not always carried out according to guidelines, especially in young adults.
- The incidence of hypoglycaemia is high in teenagers and young adults.
- The incidence of hypokalaemia in young adults is high.

advised. Guidance on fluid type and potassium replacement is also given [11].

Alongside a national survey of the management of diabetic ketoacidosis in adults against the standards in the JBDS guidelines, the results of which have been reported elsewhere [12], we also conducted a survey of the management and outcomes of diabetic ketoacidosis in teenagers in paediatric services. The aim of this joint survey was to examine the quality of management of young people (aged < 22 years) against the JBDS guidelines [10] in adult services, and the BSPED guidelines [3] for paediatric services, and to study the differences in management and outcomes.

## **Research design and methods**

A data collection questionnaire was developed using the 2013 JBDS guideline as a template [10]. The questionnaire was adapted slightly for paediatric services as some questions were not appropriate, although the majority remained the same (Appendices S1 and S2).

Adult services were identified through the databases of Diabetes UK, the Association of British Clinical Diabetologists and the Diabetes Inpatient Specialist Nurse UK Group. Paediatric diabetes services were identified through the Regional Paediatric Diabetes Networks and the Association of Children's Diabetes Clinicians. The questionnaires were sent out by e-mail to all 220 UK specialist adult diabetes teams and 185 paediatric diabetes services in England and Wales. One clinician from each service was asked to fill in a single form for each of the subsequent five patients at their institution (for paediatrics, those aged > 14 years) with a diagnosis of diabetic ketoacidosis and return them between May and December 2014.

For this comparison of teenage and young adults with diabetic ketoacidosis, all the paediatric responses were included as well as the adult responses relating to young people aged  $\leq 22$  years. These are termed 'paediatric' and 'adult', regardless of the age of the patient.

We used *t*-tests and ANOVA for comparisons between groups.

The Clinical Audit and Improvement Department of the Norfolk and Norwich University Hospitals NHS Foundation Trust deemed the present survey to be a service improvement exercise and confirmed that the project did not require multisite ethical, research governance or audit approval.

## Results

#### **Clinical details**

For paediatric patients, 71 forms were received from 56 hospitals. Each form represented an individual admission for a unique patient. The mean (SD) patient age was 14.9 (1.4) years. For adult patients, of the 283 forms received in the full adult survey, 64 patients were aged  $\leq 22$  years. The mean (SD) age of this group was 19.2 (2.3) years. Adult physicians reported that seven younger teenagers aged 10–16 years received diabetic ketoacidosis management from adult teams. These children and young people were cared for in adult environments using the adult guidelines.

The participating hospitals reporting these patients are listed in Appendix S3. The forms were completed by a mix of consultants, trainees and diabetes specialist nurses.

The median [interquartile range (IQR)] length of stay for the paediatric patients was 1.85 (1.00, 2.74) days, with a mean (sD) of 2.35 (2.3) days, and in the adult patients it was 2.0 (1.12, 2.67) days, with a mean (sD) of 2.53 (2.4) days (P = 0.3). One paediatric patient and six adult patients developed diabetic ketoacidosis as an existing inpatient. Table 1 shows the clinical sites of care of the patients.

A total of 37.2% of the paediatric patients and 42.2% of adult patients had at least one previous admission for diabetic ketoacidosis in the preceding 12 months (median 2, range 1–7). The reasons for admission for diabetic ketoacidosis are shown in Table 2. Only one paediatric patient (1.6%) and three adult patients (4.7%) in these cohorts had diabetic ketoacidosis as a new presentation of Type 1 diabetes.

 Table 1 Care setting in paediatric patients compared with adult patients

|                           | Paediatric<br>patients,<br>% ( <i>n</i> = 71) | Adult patients $(n = 64)$ % |  |  |
|---------------------------|---|-----------------------------|--|--|
| Gender                    |   |                             |  |  |
| Male                      | 53.5  | 50                          |  |  |
| Female                    | 46.5  | 50                          |  |  |
| Treatment area            |   |                             |  |  |
| Level 1 (general ward)    | 21.4  | 10.9                        |  |  |
| Level 2 (high dependency) | 41.4  | 12.5                        |  |  |
| Level 3 (intensive care)  | 2.9%  | 12.5                        |  |  |
| Acute medical unit        | 5.7   | 43.8                        |  |  |
| Accident and emergency    | 18.6  | 10.9                        |  |  |
| Combination               | 8.6   | 9.4                         |  |  |
| Missing data              | 1.4   | 0                           |  |  |

Bold values indicate major differences.

#### Diagnosis criteria and adherence to guidelines

The mean ( $\pm$ sD) pH at admission was 7.17 ( $\pm$ 0.19) in paediatric and 7.15 ( $\pm$ 0.20) in adult patients. The mean

 
 Table 2 Precipitating cause for the episode of diabetic ketoacidosis in paediatric patients compared with adult patients (more than one cause in some patients)

| Precipitating cause of diabetic<br>ketoacidosis identified | Paediatric<br>patients,<br>n (%)<br>N = 62 | Adult<br>patients,<br><i>n</i> (%)<br><i>N</i> = 50 |  |
|--|--|---|--|
| New diabetes diagnosis                                     | 1 (1.4)                                    | 3 (4.5)   |  |
| Infection  | 9 (12.7)                                   | 14 (21.9  |  |
| Alcohol  | 2 (2.8)                                    | 4 (6.3)   |  |
| Gastroenteritis  | 7 (9.9)                                    | 9 (14.1   |  |
| Non-adherence  | 37 (52.1)                                  | 16 (25)   |  |
| Appendicitis/pancreatitis                                  | 0  | 2 (3.1)   |  |
| Insulin pump problems                                      | 5 (7.0)                                    | 0   |  |
| Psychological including<br>anorexia                        | 2 (2.8)                                    | 3 (4.5)   |  |
| No precipitating cause identified                          | 8 (11.3)                                   | 13 (20.3)   |  |

Bold values indicate major differences.

(±sD) plasma glucose concentration was 25.0 (±6.9) mmol/l in paediatric and 26.8 (±8.5) mmol/l in adult patients, and the mean (±sD) bicarbonate level was 11.3 (±4.3) mmol/l in paediatric and 11.0 (±4.7) mmol/l in adult patients. The mean (±sD) blood ketone level was 5.65 (±1.15) mmol/l in paediatric and 5.45 (±1.44) mmol/l in adult patients. There were no differences between the paediatric and adult patients in any of these criteria. There were no blood ketone measurements for 11 of the paediatric patients and nine of the adult patients.

Four paediatric patients and seven adult patients had a pH of  $\geq$  7.3 but only one adult patient did not have diabetic ketoacidosis on any criterion. One paediatric patient had a pH > 7.3, bicarbonate of > 15 but no blood ketone measurement although urine ketones of 4 + . These patients were still included in the analysis because their management was the same as that of the remaining patients.

Details of treatment given and investigations carried out during the first 24 h are shown in Table 3. National guidelines were reported to have been followed by 96% of paediatric and 87% of adult units; however, only 60 paediatric patients (84.5%) were treated according to

Table 3 Management of paediatric and adult patients in the first hour after diagnosis of diabetic ketoacidosis

| Variable   | Paediatric reports ( $N = 71$ ) |       |                          | Adult reports $(N = 64)$ |       |                         |  |
|--|---------------------------------|-------|--------------------------|--------------------------|-------|-------------------------|--|
|  | Yes, %                          | No, % | Missing or n/a,<br>n (%) | Yes, %                   | No, % | Missing or n/a<br>n (%) |  |
| Was the diagnosis made using JBDS criteria?              | 77.5                            | 1.4   | 15 (21.1)                | 59.4                     | 1.6   | 25 (39.0)               |  |
| Seen by ICU or a senior within 12 h of admission?        | 76.1                            | 18.3  | 4 (5.6)                  | 84.4                     | 6.2   | 6 (9.3)                 |  |
| Was care given according to BSPED/JBDS guidelines?       | 84.5                            | 9.6   | 4 (5.6)                  | 76.6                     | 14.1  | 6 (9.3)                 |  |
| Was the care given in an appropriate area?               | 100                             | 0     | 0                        | 93.4                     | 3.1   | 2 (3.1)                 |  |
| Was a bolus insulin dose given?                          | n/a                             | n/a   | n/a                      | 17.2                     | 78.1  | 3 (4.7)                 |  |
| Was a fixed-rate insulin infusion used?                  | 98.6                            | 1.4   | 0                        | 95.3                     | 4.7   | 0                       |  |
| Was the insulin infusion started at 0.05 units/kg/h?     | 12.9                            | 87.1  | 0                        | n/a                      | n/a   | n/a                     |  |
| Was the insulin infusion started at 0.1 units/kg/h?      | 87.1                            | 12.9  | 0                        | 100                      | 0     | 0                       |  |
| Was a bolus of 0.9% sodium chloride solution given?      | 63.4                            | 32.4  | 3 (4.3)                  | n/a                      | n/a   | n/a                     |  |
| Was intravenous 0.9% sodium chloride solution used?      | 98.6                            | 1.4   | 0                        | 98.4                     | 1.6   | 0                       |  |
| Potassium replacement in accordance with local protocol? | 93.0                            | 4.2   | 2 (2.8)                  | 82.8                     | 9.4   | 5 (7.8)                 |  |
| Early warning score recorded?                            | 74.7                            | 14.1  | 8 (11.3)                 | 90.6                     | 6.3   | 2 (3.1)                 |  |
| Respiratory rate recorded?                               | 91.6                            | 0     | 6 (8.4)                  | 98.4                     | 0     | 1(1.6)                  |  |
| Temperature recorded?                                    | 91.6                            | 0     | 6 (8.4)                  | 98.4                     | 0     | 1(1.6)                  |  |
| Pulse rate recorded?                                     | 91.6                            | 0     | 6 (8.4)                  | 100                      | 0     | 0                       |  |
| Oxygen saturations recorded?                             | 91.6                            | 0     | 6 (8.4)                  | 100                      | 0     | 0                       |  |
| Glasgow coma scale recorded?                             | 98.6                            | 1.4   | 0                        | 90.6                     | 6.3   | 2(3.1)                  |  |
| Full history recorded?                                   | 100                             | 0     | 0                        | 96.9                     | 3.1   | 0                       |  |
| Full examination recorded?                               | 100                             | 0     | 0                        | 89.1                     | 4.7   | 4 (6.2)                 |  |
| Blood ketones recorded?                                  | 91.6                            | 8.4   | 0                        | 89.1                     | 10.9  | 0                       |  |
| Capillary blood glucose recorded?                        | 97.2                            | 2.8   | 0                        | 98.4                     | 1.6   | 0                       |  |
| Venous plasma glucose recorded?                          | 88.7                            | 7.0   | 3 (4.2)                  | 96.9                     | 1.6   | 1(1.6)                  |  |
| Urea and electrolytes recorded?                          | 98.6                            | 1.4   | 0                        | 100                      | 0     | 0                       |  |
| Venous blood gases recorded?                             | 93.0                            | 7.0   | 0                        | 90.6                     | 7.8   | 1(1.6)                  |  |
| Full blood count performed?                              | 97.2                            | 1.4   | 1 (1.4)                  | 90.6                     | 3.1   | 4 (6.3)                 |  |
| ECG performed?   | 23.9                            | 63.4  | 9 (12.7)                 | 73.4                     | 20.3  | 4 (6.3)                 |  |
| Chest X-ray performed?                                   | 12.7                            | 77.5  | 7 (9.9)                  | 64.1                     | 28.1  | 5 (7.8)                 |  |
| Urine analysis performed?                                | 78.9                            | 18.3  | 2 (2.8)                  | 67.2                     | 20.3  | 8 (12.5)                |  |

BSPED, British Society of Paediatric Endocrinology and Diabetes; ECG, electrocardiogram; ICU, intensive care unit; JBDS, Joint British Diabetes Societies; n/a, not applicable.

Bold values indicate major differences.

BSPED guidelines (seven were not and four were missing), and only 49 adult patients (76.6%) were treated according to JBDS guidelines (nine were not and six were missing).

#### Fluid

Intravenous 0.9% sodium chloride solution was first started a median (IQR) of 34 (18, 78) min after admission in paediatric patients and 36 (15, 80) min after admission in adult patients. A total of 45 of the paediatric patients were given a 0.9% sodium chloride bolus dose (their mean pH was 7.14  $\pm$  0.15) and 23 were not (mean pH 7.23  $\pm$  0.05; *P* = 0.005). Table 3 summarizes the diagnosis and management of the patients during the first hour after admission. Senior review (by a registrar or consultant) occurred within the first 12 h in 76% of paediatric patients and 84% of adult patients.

#### Insulin

An insulin bolus was given to 11 adult patients (17%); two of these had severe diabetic ketoacidosis with a pH of < 7.1, and two were aged < 18 years. Bolus doses were not used in paediatric care. The median (IQR) time from diagnosis to starting intravenous insulin infusion was 39 (19, 72) min in adult patients and 100 (84, 116) min in paediatric patients (P < 0.001). Of the paediatric patients, 61 were started on an infusion rate of 0.1 units/kg/h, and nine were started at a rate of 0.05 units/kg/h. Although the mean pH of the two groups was no different (7.17 ± 0.02 vs 7.14 ± 0.04; P = 0.26), those treated with 0.05 units/kg/h took significantly longer to reach diabetic ketoacidosis resolution (median 21.4 vs 15.3 h; P = 0.015). The small group given the lower insulin dose were younger (13.9 ± 2.4 years) than the larger group receiving the higher dose (15.0 ± 1.8 years; P < 0.02). As the majority of the adult patients were treated according to the JBDS guidelines, it was assumed that the insulin infusion was given at a rate of 0.1 units/kg/h. Their median time to resolution was 18.2 h.

In patients already using long-acting insulin, this was more likely to be continued in adult patients (88%) than in paediatric patients (45%).

#### Biochemical changes during the first 24 h

#### Glucose

A total of 44% of the paediatric patients and 36% of the adult patients became hypoglycaemic (blood glucose levels < 4.0 mmol/l) during the first 24 h of treatment, and 18/57 adult patients (32%) became hypoglycaemic if the glucose concentration in the intravenous fluid was changed to 10% when blood glucose fell to 14 mmol/l, but 5/7 patients (71%) became hypoglycaemic if 10% glucose was not used. In paediatric patients, the glucose concentration was changed to 10% in 37 [of whom 16 (43%) became hypoglycaemic], but not in 27 patients [of whom 14 (52%) became hypoglycaemic]. None of the paediatric patients (n = 9) starting on the lower insulin infusion rate (0.05 units/kg/h) became hypoglycaemic during the first 24 h.

#### Potassium

The mean ( $\pm$ SD) potassium on admission was 4.8 ( $\pm$ 1.0) mmol/l in paediatric patients and 4.8 ( $\pm$ 0.8) mmol/l in adult patients. Figures 1 and 2 show the changes in pH and potassium values during the course of the 24 h after admission in both groups. Mean potassium levels gradually fell over the first 24 h in both groups. The mean lowest recorded potassium during the admission was 3.8 ( $\pm$  0.5) mmol/l in paediatric patients, but 3.5 ( $\pm$  0.6) mmol/l in adult patients (P < 0.005). A total of 23.6% of all potassium levels

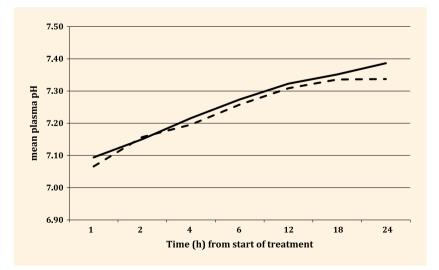


FIGURE 1 Changes in plasma pH over time. Paediatric values in the dashed line and adult values in the solid line. Results are shown as mean of all values at each h.

measured over the first 24 h in adult patients, but only 8.8% in paediatric patients were < 3.5 mmol/l (P < 0.005). Those paediatric patients starting on the lower insulin rate (0.05 units/kg/h) had no less hypokalaemia than those starting at the higher rate (14.3% compared with 7.9% total potassium levels < 3.5 mmol/l). In adult patients, lowest potassium levels were no lower in those given a bolus dose of insulin (3.8 ± 0.4 mmol/l) than in those who were not (3.5 ± 0.6 mmol/l; P = 0.2).

There was no difference in the risk of developing either hypokalaemia or hypoglycaemia between those respondents who followed the national guidelines and those who did not.

#### Monitoring during hospital admission

Table 4 shows the extent of monitoring in paediatric and adult patients; paediatric patients were more likely to receive

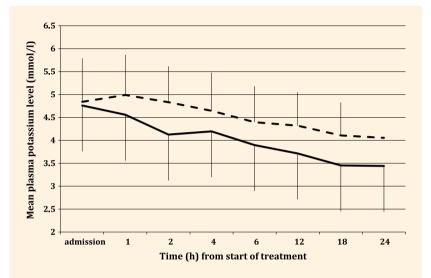


FIGURE 2 Changes in plasma potassium levels over time. Paediatric values in the dashed line and adult values in the solid line. Results are shown as mean and standard deviations of all values at each h.

Table 4 Ongoing diabetic ketoacidosis management, outcome and discharge

|  | Paediatric reports $(n = 71)$  |          |                             | Adult reports $(n = 64)$ |          |                                    |
|--|--|----------|-----------------------------|--------------------------|----------|------------------------------------|
| Variable   | Yes,<br>%  | No,<br>% | Missing<br>or n/a,<br>n (%) | Yes,<br>%                | No,<br>% | Missing<br>or n/a,<br><i>n</i> (%) |
| Was an appropriate monitoring regimen established?                               | 84.5   | 11.3     | 3 (4.2)                     | 68.8                     | 28.1     | 2 (3.1)                            |
| Capillary glucose levels measured hourly?  | 95.8   | 4.2      | 0                           | 84.4                     | 14.1     | 1 (1.6)                            |
| Ketone levels measured hourly?   | 69.0   | 31.0     | 0                           | 67.2                     | 28.1     | 3 (4.7)                            |
| Observations of vital signs taken hourly?  | 97.2   | 2.8      | 0                           | 68.8                     | 26.6     | 3 (4.7)                            |
| Early warning score measured hourly?   | 77.5   | 19.7     | 2 (2.8)                     | 62.5                     | 32.8     | 3 (4.7)                            |
| Urine output documented?   | 71.8   | 25.4     | 2(2.8)                      | 68.8                     | 26.6     | 3 (4.7)                            |
| If patient was already on long-acting insulin, was this continued?               | 45.1<br>(n = 53)   | 29.6     | 0                           | 88.4 $(n = 43)$          | 11.6     | 0                                  |
| Was 10% glucose started when the glucose dropped to < 14 mmol/l?                 | 52.1   | 38.0     | 7 (9.9)                     | 82.8                     | 10.9     | 4 (6.3)                            |
| Review of fluid balance with the rate of normal saline amended if appropriate?   | 67.6   | 14.1     | 13 (18.3)                   | 65.6                     | 7.8      | 17 (26.6                           |
| Did the patient ever develop hypoglycaemia?                                      | 43.7   | 56.3     | 0                           | 35.9                     | 62.5     | 1 (1.6)                            |
| If progress was not satisfactory, did a senior review occur?                     | $     \begin{array}{l}       100 \\       (n = 24)     \end{array} $ | 0        | 0                           | 100   (n = 19)           | 0        | 0                                  |
| Was the transition to subcutaneous insulin managed appropriately?                | 93.0   | 4.2      | 2(2.8)                      | 84.4                     | 10.9     | 3 (4.7)                            |
| Was a referral to diabetes team made during admission?                           | 85.9   | 5.6      | 6 (8.5)                     | 90.6                     | 3.1      | 4 (6.3)                            |
| After diabetic ketoacidosis resolution, were they reviewed by the diabetes team? | 93.0   | 7.0      | 0                           | 96.9                     | 1.6      | 1 (1.6)                            |
| Did the patient receive education support before discharge?                      | 84.5   | 12.7     | 2 (2.8)                     | 89.1                     | 1.6      | 6 (9.4)                            |
| Did the patient receive psychological support before discharge?                  | 11.3   | 80.3     | 6 (8.5)                     | 6.3                      | 84.4     | 6 (9.4)                            |

Bold values indicate major differences.

appropriate monitoring during their diabetic ketoacidosis episode.

#### Resolution of diabetic ketoacidosis and discharge planning

The median (IQR) length of time to resolution of diabetic ketoacidosis in the paediatric patients was 16.03 (10.0, 21.03) h and in the adult patients was 18.18 (9.66, 34.12) h. Table 4 shows the steps involved at the resolution of diabetic ketoacidosis and transfer onto subcutaneous insulin. The majority of paediatric and adult patients had some educational input, but very few of either group had any psychological input before discharge.

#### Discussion

The present large study is the first to compare the management of diabetic ketoacidosis in young adults and adolescents on a national basis. The quality of care was generally good in both adult and paediatric services, and the majority of patients received appropriate monitoring and treatment according to national guidelines; however, there was still a minority of adults (14%) and adolescents in paediatric care (10%) who were not treated according to national guidelines. Furthermore, it is of some concern that adult specialist diabetes services were managing diabetic ketoacidosis in a small number of children down to 10 years old using adult guidelines. In addition, a significant proportion of each group developed hypoglycaemia and/or hypokalaemia during treatment.

The identified precipitating causes were different between the groups, with non-adherence identified in around half of the paediatric patients, but only a quarter of the adult patients. The fact that 37% of the paediatric group and 42% of the adult patients had experienced at least one episode of diabetic ketoacidosis in the previous 12 months (with seven admissions in one patient) suggest that many of the admissions are a result of non-adherence, even though adult patients are more likely to be recorded with 'gastroenteritis'. Investigation routinely includes a chest X-ray in the adult patients, although none was reported to have pneumonia or any other condition which would be identified on a chest Xray. In young adults aged < 22 years, this could be removed from the guidelines as a routine investigation, but left to clinical discretion, as in children.

In the National Paediatric Diabetes Audit, around a third of diabetic ketoacidosis episodes were recorded at the diagnosis of diabetes [13]; however, in the present survey, only four patients (3.0%) were newly diagnosed. This is a very low number, but could be attributable to the fact that young people aged  $\geq$  14 years are less likely to present with diabetic ketoacidosis at diagnosis than younger children (4– 11% compared with 23–15% in children aged < 4 years [13]). Seven patients (one paediatric and six adult) developed diabetic ketoacidosis as an existing inpatient. This is clearly a major safety concern. This has been identified as a particular problem in the National Diabetes Inpatient Audit in adults [1] and is currently the focus of improved training of ward nurses and junior doctors in the importance of monitoring of diabetes and adequate insulin replacement [14].

Although a large randomized study of various fluid regimes in paediatric patients is currently underway in the USA [15], in the UK the use of 0.9% sodium chloride solution ('normal saline') is now almost universal in both adult and paediatric services. In the paediatric patients, those receiving a sodium chloride bolus had a lower pH.

A small number of adult patients (17%) received an insulin bolus, despite guidelines that do not recommend it, and two of these patients were aged < 18 years. This is not appropriate treatment because in patients aged < 18 years, the JBDS recommends that the paediatric BSPED guideline is followed, which advises against a bolus dose of insulin because it is unnecessary and, in this age group, it can increase the risk of cerebral oedema [7]. Furthermore, paediatric guidelines recommend a delay in starting insulin for at least 1 h after starting intravenous fluids, because early insulin has been shown to increase the risk of cerebral oedema [7]. This recommendation was being followed in the paediatric patients who started insulin 100 min after admission, compared with 39 min in the adult patients, but this is another concern for children who are being treated according to adult guidelines.

Not all patients, either adult or paediatric, appear to have been seen by senior doctors during the early management. Only 69% of responders felt that an appropriate monitoring strategy had been established in the adult patients (compared with 85% in the paediatric patients); lower rates of regular monitoring of capillary glucose and vital signs were recorded in adults. A total of 90% of all patients had their blood ketone levels measured initially, but only 60% repeatedly through the episode.

One third of all patients, both paediatric and adult, developed hypoglycaemia. In adult patients hypoglycaemia has been shown to be a strong predictor of longer length of hospital stay and mortality [16]. This suggests that either the insulin dose (fixed rate or bolus) was excessive. None of the paediatric patients started on the 0.05 units/kg/h insulin infusion developed hypoglycaemia, but in order to convincingly answer the question of which dose is safer, a randomized controlled trial of 0.1 units/kg/h compared with 0.05 units/kg/h needs to be carried out in both children and young adults [17,18]. In addition, a much smaller number of paediatric patients were changed to 10% glucose (52 vs 80% of adults) when their blood glucose level fell.

Hypokalaemia also occurred in large numbers of patients, but there was more than twice the incidence of hypokalaemia in the adult compared with the paediatric patients, although there was no evidence of harm. Both the JBDS and BSPED guidelines suggest adding 40 mmol potassium per litre of intravenous fluid, but the JBDS guidelines recommend that no potassium be prescribed if the serum potassium level remains > 5.5 mmol/l and it should only be added if the patient is passing urine [9]. Because most of the difference in the fall of blood potassium levels that we observed occurred during the first 2 h of treatment (Fig. 2), it is possible that the delay while waiting for urine to be produced may be important. The delay in starting the insulin infusion for at least 1 h after the start of intravenous fluids may also help to prevent an early fall in potassium levels in the paediatric patients.

The majority of paediatric and adult patients (> 90%) were referred to and seen by the diabetes team before discharge; however, the vast majority of all children and young people did not receive psychological support before discharge. The provision of this service is known to be lacking in many teams, although generally advocated as an important part of a diabetes team. The higher rate of paediatric psychology input compared with the adult services (11.4 vs 5.6%) may be a reflection of the increased psychology provision through the Best Practice Tariff in England [19]. It would be very beneficial if this tariff could also be extended to adult services for young people up to the age of 25 years, especially as a high proportion of the episodes of diabetic ketoacidosis are related to adherence difficulties.

A limitation of the present study is that we asked for voluntary contributions from teams across the UK, and for unselected sequential cases, but come case selection may have occurred. Despite this, we feel that the forms returned are likely to be a good representation of patients presenting daily to emergency adult teams and paediatric services across the UK and elsewhere, and this is the largest study of its kind reported. This survey was not designed to look at prevalence or risk factors of diabetic ketoacidosis, but rather at the quality of management.

In summary, the present data represent the largest ever nationwide survey on the management of diabetic ketoacidosis. For the first time this has allowed a comparison of the management and outcomes in adolescents and young people from the age of 14 to 22 years, managed in paediatric and adult services. Although guidelines are largely followed in both groups, we have highlighted a small group of children being treated according to adult guidelines, which is a concern. There is a significant risk of hypokalaemia in the adult patients and of hypoglycaemia in both groups. This suggests that the potassium and glucose replacement regimens, and insulin replacement, need to be studied further in randomized trials in both paediatric and adult services. We recommend that adult and paediatric teams work together to produce the safest guidelines for adolescents and young adults, who may have different requirements from older adults.

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#### Competing interests

None declared.

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## References

- 1 Health and Social Care Information Centre. National Diabetes Inpatient Audit (NaDIA), Open data - 2013. Available at http:// www.hscic.gov.uk/catalogue/PUB14358 Last accessed 16 July 2015.
- 2 Faich GA, Fishbein HA, Ellis SE. The epidemiology of diabetic acidosis: a population-based study. *Am J Epidemiol* 1983; 117: 551–558.
- 3 British Society of Paediatric Endocrinology and Diabetes. Guidelines for the management of diabetic ketoacidosis 2009 (minor review 2013). Available at http://www.bsped.org.uk/clinical/docs/DKAGuideline.pdf Last accessed 16 July 2015.
- 4 Edge JA, Ford-Adams ME, Dunger DB. Causes of death in children with insulin dependent diabetes 1990–1996. Arch Dis Child 1999; 81: 318–323.
- 5 Glaser N, Barnett P, McCaslin I, Nelson D, Trainor J, Louie J et al. Risk factors for cerebral edema in children with diabetic ketoacidosis. N Eng J Med 2001; 344: 264–269.
- 6 Muir AB, Quisling RG, Yang MC, Rosenbloom AL. Cerebral edema in childhood diabetic ketoacidosis: Natural history, radiographic findings, and early identification. *Diabetes Care* 2004; 27: 1541–1546.
- 7 Edge JA, Jakes RW, Roy Y, Hawkins M, Winter D, Ford-Adams ME *et al.* The UK case–control study of cerebral oedema complicating diabetic ketoacidosis in children. *Diabetologia* 2006; **49**: 2002–2009.
- 8 Savage MW, Sinclair-Hammersley M, Rayman G, Courtney H, Dhatariya K, Dyer P *et al.* The management of diabetic ketoacidosis in adults. Available at http://www.diabetologists-abcd.org.uk/ JBDS/JBDS\_IP\_DKA\_Adults.pdf Last accessed 16 July 2015.
- 9 Savage MW, Dhatariya KK, Kilvert A, Rayman G, Rees JA, Courtney CH et al. Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. *Diabetic Med* 2011; 28: 508–515.
- 10 Dhatariya K, Savage M. Joint British Diabetes Societies Inpatient Care Group. The management of diabetic ketoacidosis in adults.

Second edition. Update: September 2013. Available at http:// www.diabetologists-abcd.org.uk/JBDS/JBDS\_IP\_DKA\_Adults\_ Revised.pdf Last accessed 16 July 2015.

- 11 Dhatariya K. The evolution of DKA management. Br J Diabetes Vasc Dis 2015; 15: 31–33.
- 12 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**: 252–260.
- 13 Royal College of Paediatrics and Child Health. National Paediatric Diabetes Audit 2013-14. Part 1. Care processes and outcomes. Available at http://www.rcpch.ac.uk/system/files/protected/page/ 2014%20NPDA%20Report%201%202014%20FINAL.pdf Last accessed 16 July 2015.
- 14 Virtual College. The safe use of insulin 2014 update e learning module. Available at http://www.virtual-college.co.uk/products/ safe-insulin.aspx Last accessed 16 July 2015.
- 15 Glaser NS, Ghetti S, Casper TC, Dean JM, Kupperman N. Pediatric diabetic ketoacidosis, fluid therapy, and cerebral injury: the design of a factorial randomized controlled trial. *Pediatr Diabetes* 2013; 14: 435–446.
- 16 Garg R, Hurwitz S, Turchin A, Trivedi A. Hypoglycemia, with or without insulin therapy, is associated with increased mortality among hospitalized patients. *Diabetes Care* 2013; 36: 1107–1110.

- 17 Puttha R, Cooke D, Subbarayan A, Odeka E, Ariyawansa I, Bone M *et al.* Low dose (0.05 units/kg/h) is comparable with standard dose (0.1 units/kg/h) intravenous insulin infusion for the initial treatment of diabetic ketoacidosis in children with type 1 diabetes—an observational study. *Pediatr Diabetes* 2010; **11**: 12–17.
- 18 Al Hanshi S, Shann F. Insulin infused at 0.05 versus 0.1 units/kg/hr in children admitted to intensive care with diabetic ketoacidosis. *Pediatr Crit Care Med* 2011; 12: 137–140.
- 19 Department of Health (2015) Payment by Results. Guidance for 2013-14. Available at https://www.gov.uk/government/uploads/ system/uploads/attachment\_data/file/214902/PbR-Guidance-2013-14.pdf Last accessed 16 July 2015.

## **Supporting Information**

Additional Supporting Information may be found in the online version of this article:

Appendices S1 and S2 Questionnaires sent to all adult and paediatric diabetes teams in all UK hospitals. Appendix S3 List of all contributing hospitals.