

Research: Health Economics

The cost of treating diabetic ketoacidosis in an adolescent population in the UK: a national survey of hospital resource use

K. K. Dhatriya^{1,2} , K. Parsekar³, C. Skedgel³, V. Datta⁴, P. Hill⁴ and R. Fordham³

¹Elsie Bertram Diabetes Centre, Norfolk and Norwich University Hospitals NHS Foundation Trust, ²Norwich Medical School, ³Health Economics Consulting, Norwich Medical School, University of East Anglia and ⁴Diabetes Department, Jenny Lind Children's Hospital, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK

Accepted 4 January 2019

Abstract

Aims Adolescents with Type 1 diabetes commonly experience episodes of ketoacidosis. In 2014, we conducted a nationwide survey on the management of diabetic ketoacidosis in young people. The survey reported how individual adolescents with diabetes were managed. However, the costs of treating diabetic ketoacidosis were not reported.

Methods Using this mixed population sample of adolescents, we took a 'bottom-up' approach to cost analysis aiming to determine the total expense associated with treating diabetic ketoacidosis. The data were derived using the information from the national UK survey of 71 individuals, collected via questionnaires sent to specialist paediatric diabetes services in England and Wales.

Results Several assumptions had to be made when analysing the data because the initial survey collection tool was not designed with a health economic model in mind. The mean time to resolution of diabetic ketoacidosis was 15.0 h [95% confidence interval (CI) 13.2, 16.8] and the mean total length of stay was 2.4 days (95% CI 1.9, 3.0). Based on data for individuals and using the British Society of Paediatric Endocrinology and Diabetes (BSPED) guidelines, the cost analysis shows that for this cohort, the average cost for an episode of diabetic ketoacidosis was £1387 (95% CI 1120, 1653). Regression analysis showed a significant cost saving of £762 (95% CI 140, 1574; $P = 0.04$) among those treated using BSPED guidelines.

Conclusion We have used a bottom-up approach to calculate the costs of an episode of diabetic ketoacidosis in adolescents. These data suggest that following treatment guidelines can significantly lower the costs for managing episodes of diabetic ketoacidosis.

Diabet. Med. 36, 982–987 (2019)

Introduction

Ketoacidosis is a frequently encountered metabolic emergency in adolescents with Type 1 diabetes [1]. Recent work has shown that each episode of diabetic ketoacidosis (DKA) in an adult in the UK in 2014 cost the National Health Service (NHS) £2064 per person [95% confidence interval (CI) 1800, 2563] [2]. However, the costs of DKA in young people remain unknown.

In 2014, a national survey was carried out in the UK looking at the management of DKA in adolescents and young adults aged between 11 and 22 years [3]. This survey looked at outcomes of a convenience sample of young people with

diabetes aged < 18 years (mean age 14.9 years, range 11–18) presenting with DKA over a 7-month period. Some 56 of 185 paediatric diabetes services returned data on 120 admissions looking at all aspects of their care during the acute hospital admission [3]. Each admission was for a separate individual. The demographic data for these individuals have been described previously [3]. We used this data set to assess how much it cost to treat DKA in young people in the UK in 2014.

Methods

Our analysis was identical to that used in our previous work on the costs of adult DKA [2]. The cost analysis followed a bottom-up approach and was based on an aggregation of individual-level factors collected as part of the questionnaire,

Correspondence to: Ketan Dhatriya. E-mail: ketan.dhatriya@nuh.nhs.uk

What's new?

- Adolescents with Type 1 diabetes frequently experience diabetic ketoacidosis. However, how much treating this condition costs in this age group remains unknown in the UK.
- We used the 2014 national survey data set to conduct a novel, 'bottom-up' approach to cost analysis.
- Our data suggest that the average cost of an episode of diabetic ketoacidosis in an adolescent in the UK in 2014 was £1387.
- Use of the British Society of Paediatric Endocrinology and Diabetes guidelines was associated with a significant £762 reduction in costs.

and informed by the 2013 British Society of Paediatric Endocrinology and Diabetes (BSPED) guidelines [4]. This is the version of the guidelines that would have been used for those presenting with DKA at the time of the data collection. The main components of our cost estimates included laboratory and diagnostic assessments, physician and nurse contacts, as well as drug dosages during the early phase of the DKA admission. Following resolution of DKA per diem ward costs were used. We used questionnaires to estimate the number of diagnostic tests, as well as time from admission to DKA resolution and time to discharge. The times taken by healthcare professionals were based on expert opinion. Our costing assumptions are shown below, and individual prices are shown in Table 1.

- Individuals were assessed on admissions for 15 min by a junior doctor.
- On admission, a nurse took 15 min to collect urine and blood samples.
- Everyone received intravenous insulin according to BSPED guidelines every hour from admission to DKA resolution. This required 5 min of junior doctor time and 15 min of nurse time per hour.
- For dosing purposes, individuals were assumed to weigh an average of 55 kg; the mean weight at the 50th centile of boys (56 kg) and girls (54 kg) aged 14.9 years [10].
- It took 30 min of nurse time to be assessed by members of the paediatric diabetes specialist team.
- Table 2 shows the location of care during the DKA phase as recorded in the individual questionnaires. It was assumed that, when their DKA had resolved, individuals were transferred to a general paediatric ward for the remainder of their hospital stay.
- If there were more than one treatment location recorded (7% of responses), we assumed treatment occurred in the more intensive location.

Table 1 Cost components (unit prices)

Cost component	Unit cost (£)
Hospital facilities	
Level 1: general ward (per day)	428.49*
Level 2: high-dependency unit (per day)	889.14*
Level 3: intensive treatment unit (per day)	2004.45*
Acute medical unit (per day)	428.49*
Accident and Emergency (per day)	2552.00*
Other wards (per day)	428.49*
Healthcare staff (per hour)	
Staff nurse (band 6)	13.32 [†]
Specialist registrar (middle band)	23.76 [‡]
Junior doctor	14.39 [‡]
Diabetes specialist nurse (band 6)	16.70 [†]
Investigations	
X-ray	25.00 [§]
Laboratory blood tests	1.00 [§]
Electrocardiogram (ECG)	32.00 [§]
Urine test strip (per 10)	4.30 [¶]
Intravenous insulin	5.24**
1 litre 0.9% sodium chloride solution with potassium	2.20 ^{††}

Data taken from *Welsh Government [5], [†]Royal College of Nursing [6], [‡]NHS Employers [7], [§]Department of Health [8], [¶]Medisupplies (<https://www.medisupplies.co.uk/Diagnostic-Equipment/Blood-Urinalysis-Testing/Urinalysis-Testing/Bayer-Multistix-Diagnostic-Strips>), **British National Formulary [9], ^{††}MedicinesComplete (https://www.medicinescomplete.com/mc/bnf/current/PHP87990-potassium-chloride-with-sodium-chloride.htm?q=Potassium&t=search&css=text&tot=543&p=6#_hit).

- Unlike adults, there is no target for the length of time young people spend in an emergency department, thus for those treated in Accident and Emergency or a paediatric assessment unit, we assumed a maximum time of 4 h after which they were equally likely to be transferred to paediatric intensive care unit or the general ward until DKA resolution.
- We used published data to calculate the per diem costs for time on the acute wards and time spent in the general ward according to the best practice tariff [5,11].
- We assumed 30 min of nurse time for a follow-up visit from the paediatric specialist diabetes team.

A bottom-up costing approach involves resource utilization at the patient or individual level. The patient-level utilization data are aggregated to identify types of resources used to calculate overall costs. In contrast to a bottom-up approach, top-down costing first calculates the total costs of the service at the organizational, provider or departmental level and then disaggregates the total costs to the department or the units of service or products [12].

We used the sum of individual components to calculate the total costs. These included the costs of initial assessments by the medical and nursing staff as well as diagnostic/laboratory tests, insulin and other drugs during the acute

Table 2 Distribution of individuals by treatment area, with the differences in costs for the BSPED vs. non-BSPED groups

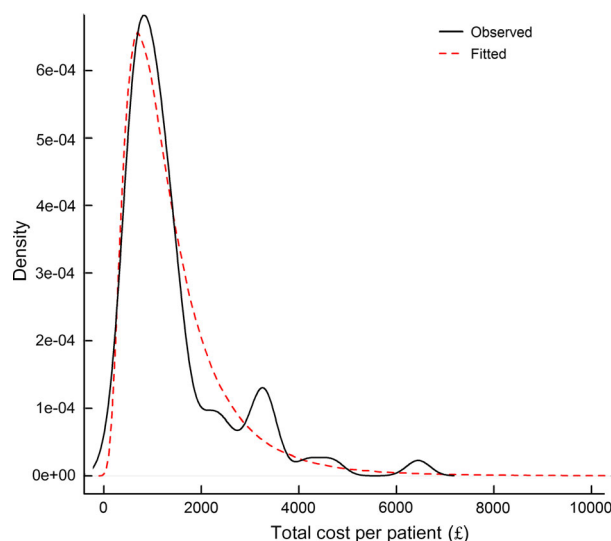
Treatment area distribution (%)	Follow BSPED (n = 60)	Don't follow BSPED (n = 11)
High-dependency unit	47	27
General ward	22	18
Accident and Emergency	22	0
Assumption made	0	45*
Acute medical unit	5	9
Intensive treatment unit	3	0
Other	2	0
Total costs (mean)	£1294	£2151
(95% confidence interval)	(1065, 1523)	(869, 3432)
Mean difference		
95 percent confidence interval	£140, £1574	

BSPED, British Society of Paediatric Endocrinology and Diabetes; * Assumption made for five cases here which reported treatment in high-dependency unit, acute medical unit or intensive treatment unit along with Accident and Emergency.

DKA phase. In addition, ward per diem costs during the acute phase of treatment, and during recovery, as well as a follow-up visit post admission were estimated. We did not include costs associated with the consequences of the episode or treatment of any precipitating factors. We also did not include costs associated with any follow-up beyond an initial visit from a member of the paediatric diabetes specialist team.

Missing data and imputation

We used multiple imputation methods to infer values for missing values, assuming values were missing completely at random [2]. This was because a number of variables had a high proportion of missing values. We performed predictive mean matching using the Multivariate Imputation by Chained Equations Package in R statistical software (version 3.4.2) [13]. This method estimates a regression model for each variable with missing values, and replaces each missing value with the value of the record with the closest match on the regressed predictors [14]. The regression model is used to estimate the similarity of the record with other non-missing observations rather than the missing value itself. Table S1 shows a summary of the questionnaire data as well as the variables with imputed values. Table S2 lists the costs by individual component. We did not impute non-continuous variables including flags indicating any particular imaging modality or blood test. Rather, we imputed the continuously distributed subtotals for the individual components, i.e. nursing and physician times; laboratory or other diagnostic tests; insulin and other drugs; and ward per diems. We used the sum of these components to estimate total cost. This allowed us to avoid using strong assumptions about the distribution of non-normal parameters but rather as much as possible used the estimated total cost to be based on observed

**FIGURE 1** Comparison of the observed and imputed total costs

values. A comparison of the observed and imputed total costs is shown in Fig. 1.

Following data imputation, we tested the fit of different theoretical distributions to inform future modelling efforts. We tested gamma and log-normal distributions using the fitdistrplus package and selected the preferred distribution on the basis of the Bayesian Information Criterion (BIC).

Predictors of cost and length of stay

We used linear regression to test a number of predictors of cost and length of stay. These included gender, age, number of prior admissions with DKA, flags suggesting hypoglycaemia following resolution of DKA, and whether DKA treatment followed BSPED guidelines.

Clinical care staff

We sought expert opinion from a consultant in paediatric diabetes medicine (VD) and a paediatric diabetes specialist nurse (PH) to determine the amount of time spent by medical, nursing and other clinical care staff in managing those individuals presenting with DKA. We determined minimum times that would be spent by individual members of the clinical staff. A full list of clinical staff, their allocated time, and any procedures and is provided in Appendix S1. This was constructed by the two authors (VD and PH) using the BSPED DKA guideline [4].

Similarly, we determined the hourly wage rates of a range of different staff to enable the determination of any costs associated with clinical care staff time. Sources of salaries and other costs are provided in Table 1.

Costs of DKA were considered only from the time of admission to the resolution of DKA. This allowed us to determine the impact of DKA alone on the NHS and did not take into account other factors, such as comorbidities or

individual circumstances. These may have led to higher overall costs due to lengthier hospital stays than would be the case with treating DKA alone.

Results

The mean cost per episode of DKA was £1387 (95% CI 1120, 1653), including nursing and medical time, diagnostic and laboratory assessments, intravenous insulin and ward per diems. The mean time to resolution of DKA was 15.0 h (95% CI 13.2, 16.8) and the mean total length of stay was 2.4 days (95% CI 1.9, 3.0).

We found that a theoretical log normal distribution, with a log mean of 6.999 and a standard error of 0.08, had the best fit with observed (imputed) distribution of total costs (BIC 1145.1) compared with gamma distribution (BIC 1161.4). Figure 2 shows the empirical and theoretical distributions.

The distribution of individuals by treatment area is shown in Table 2. The majority were treated in high-dependency units (HDUs) and general wards.

Predictors of time to resolution, cost and length of stay

The presence of one or more precipitating factors increased the mean time to resolution by 6.8 h ($P = 0.001$). Resolution time also increased with year of diagnosis, by 0.5 h per year ($P = 0.01$). An episode of hypoglycaemia increased the length of stay by 1.6 days ($P = 0.01$). Following the BSPED guidelines was associated with a significant reduction in total costs, by £762 (95% CI 140, 1574; $P = 0.04$). This is shown in Fig. S1.

Transfer to a high-dependency unit

Using the BSPED guidelines, we determined the number of individuals who should have been transferred to a HDU. By

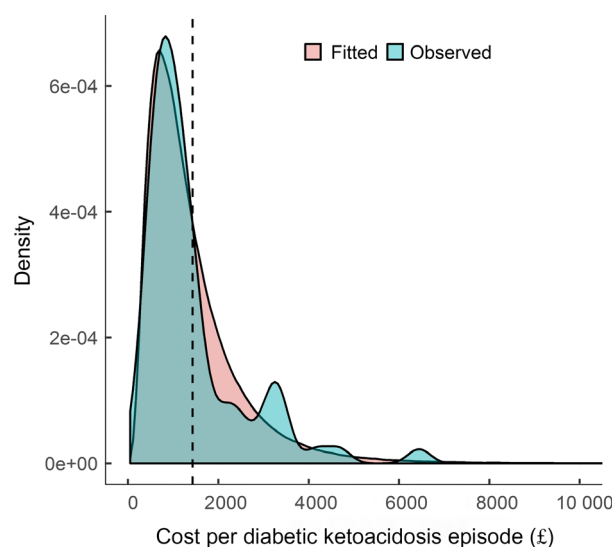


FIGURE 2 A log-normal distribution best fit the imputed total costs

observing two important factors (pH and age) we determined that according to the BSPED guidelines 46% of those with DKA should have been treated in a HDU or intensive therapy unit (ITU); however, only 26% were actually treated in HDU or ITU.

Cost impact of precipitating causes

We also looked at precipitating factors for DKA. The nationally collected data used in this analysis showed that 62 individuals (87%) provided information on their precipitating factors. Of those, 32 (52%) had poor concordance with their diabetes treatment, seven (11%) had issues with insulin pump or device failures, and 23 (37%) had a combination of other acute and non-acute illnesses. The granularity of these individual-level data are what differentiates this work from previous studies.

Discussion

This study has shown that in 2014, the average cost of treating an episode of DKA in an adolescent in the UK was £1387 (95% CI 1120, 1653), compared with £2064 (95% CI 1800, 2563) for adults [2]. In addition, we have shown that following the BSPED guidelines is associated with a £762 reduction in costs.

We acknowledge that the data gathered as part of the 2014 national survey were not specifically collected to allow for detailed health economic analyses. However, we were able to use the 2013 BSPED DKA guidelines to identify a treatment pathway that was used by the majority of hospitals who returned data [4]. In addition, using expert opinion, we were able to determine the time required by individual staff types at each step in the management pathway. Furthermore, we were able to determine the impact of a range of physiological results upon the resolution of DKA. This allowed us to be more precise in determining the costs associated with the treatment of DKA than previously.

Admissions for DKA are common in individuals under 18 years old, with reported rates of 5% per annum in Austria and Germany, 6.4% in the UK and 7.1% in the USA [15,16]. Recent data have suggested that, in the UK, the rate of DKA remained unchanged between 2012 and 2015 at just over 28% of all admissions to hospital, with about a quarter of these being children with newly diagnosed Type 1 diabetes [17]. Most episodes occur in children known to have diabetes during or after transition from the adolescent to the adult service [17,18].

Costs vary, with data from the USA in 2004 to 2014 estimating that the numbers of admissions in the USA rose by 62%, and the costs per episode of DKA also rose from \$18 987 (£15 112) to \$26 566 (£20 178) [19]. However, these were costs for all DKA admissions. Costs for children, as with the UK data, were calculated as being lower than those for adults at between \$7429 (£5642) and \$10 881 (£8264) [20]. Data from Germany did not give estimates of cost per episode, but showed that annual care costs for individuals who had

episodes of DKA were increased compared with those who did not – cost ratio of 2.2 (95% CI 2.1 to 2.3) for those with just one episode of DKA and 3.6 (95% CI 3.1 to 4.1) for those with more than one episode [16].

Cost of diabetic ketoacidosis

Direct healthcare costs

This study is one of the few to present the costs of treating DKA in adolescents from a secondary care perspective. A costing statement from the UK National Institute for Health and Care Excellence suggested that the prevention of each DKA admission was associated with a potential saving of £1000 to £1400, a figure derived from NHS England's guide to the enhanced tariff option for 2015–2016 [21]. Our data are consistent with this. One of the main reasons why the average costs for adolescent DKA were lower than a similar analysis carried out for the adult population (£1387 vs. £2064), is possibly the length of stay [2]. The median (IQR) length of stay for adolescents was 1.85 (1.00, 2.74) days, with a mean (SD) of 2.35 (2.3) days; in adults, it was 2.0 (1.12, 2.67) days, with a mean (SD) of 2.53 (2.4) days. Although this was not statistically significant ($P = 0.3$), a difference in median length of stay of 12 h may have been sufficient to account for the difference. In addition, the care setting was different, with only 2.9% of the adolescent population being in the expensive ITU, compared with 12.5% of the adult population [3,22]. Not transferring these individuals could have resulted in a lower cost of DKA treatment. Among other plausible reasons, the most significant factor to consider would be a shortage or unavailability of beds. As a result, institutional arrangement and capacity constraints might have been influential when assessing costs.

Those who were treated with the BSPED protocol incurred a significantly lower cost than those who were not. This may be because following the guidelines minimizes the room for errors and determines treatment targets. Indeed, recent work has shown that following guidelines for the management of DKA is associated with a decrease in length of stay and better prescribing, which are important determinants of cost [23].

These potential cost savings may need to be offset against the costs of nurse time, or of those providing education in terms of admissions avoidance [24]. These costs were not factored into the current model because our focus was on the cost of an episode of DKA, not on prevention or avoidance. In addition, we had no data on what contact had been made by diabetes teams with individuals prior to admission.

Productivity losses

By using forecasts of the population with diabetes increasing over the coming years and data on incidence rates of DKA, it is possible to assign values to future costs of DKA treatment. This is particularly possible using the crude prevalence rate of Type 1 diabetes mentioned in the 2017 UK National Diabetes

Paediatric Audit [25]; given as 195.4 per 100 000 of the general population in those aged 0–15 years [25]. The crude prevalence rate of DKA events in the UK was 20.1% of DKA (not at diagnosis) and 7.1% for DKA at diagnosis of Type 1 diabetes [17]. From this figure we can multiply the average cost for DKA and obtain a figure allowing us to determine the economic burden of the disease for future years. What is not taken into account by the data is the loss of productivity of caregivers/parents while their child is in hospital, and thus the overall cost to society is likely to be substantial.

We acknowledge that there are several limitations to our data. We had to make several assumptions because the data collected were not in a form that was easily usable for health economic analysis. In addition, these data came from a retrospective convenience sample. In addition, we did not add on costs associated with the treatment of comorbidities because these were so disparate and the sample size was too small to make generalized assumptions about them. Neither did we include further salary costs (e.g. employers 'on costs'). We could not cost for recurrent readmissions because none of the people included had a recurrent admission. There are already data of the costs of overall annual care in those with multiple admissions [16,26]. However, the major strengths of our data are that they were collected from across the UK, and were available from most for all stages of the patient journey – admission to resolution of DKA – from which appropriate calculations could be made.

In summary, the average cost of an episode of DKA in an adolescent in the UK in 2014 was £1387 (95% CI 1120, 1653). Although many assumptions were made to make these calculations, as the number of people with diabetes increases, it is likely that the number of people admitted with DKA will also increase. In addition, it is likely that the true costs of an episode of DKA are much higher given these many assumptions. We believe that funders can plan for future costs associated with this potentially life-threatening medical emergency using these data.

Funding sources

KP, CS and RF are employees of the University of East Anglia. KKD, VD and PH are employees of the UK National Health Service.

Competing interests

None declared.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. The differences in costs for the British Society of Paediatric Endocrinology and Diabetes (BSPED) vs. non-BSPED groups.

Table S1. Data collection with percentage of missing data and imputed data.

Table S2. Costs by component.

Appendix S1. A full list of allocated time, procedure and clinical staff needed to treat an episode of diabetic ketoacidosis.