Title:

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

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Short title: Costs of treating adolescents with DKA in the UK

Word Count: Abstract – 250   Main Manuscript – 3239

Funding: CS and RF are employees of the University of East Anglia. KKD is an employee of the UK National Health Service.

Duality of Interest The authors declare that there is no duality of interest associated with this manuscript.

Keywords: Diabetic ketoacidosis; adolescents; management; survey, costs, economic

Novelty Statement

a) Adolescents with type 1 diabetes frequently experience diabetic ketoacidosis. However, how much treating this condition costs in this age group remain unknown in the UK

b) We used the 2014 national survey dataset to conducted a novel, ‘bottom-up’ approach to cost analysis

c) Our data suggest that the average cost of an episode of diabetic ketoacidosis in an adolescent in the UK in 2014 was £1387.

d) Use of the BSPED guideline was associated with significant £762 reduction in costs.

Abstract

Aims

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

Methods

Using this mixed population sample of adolescents we used a ‘bottom up’ approach to cost analysis aiming to determine the total expense associated with treating DKA. 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 DKA was 15.0hrs (95% CI: 13.2, 16.8) and the mean total length of stay was 2.4 days (95% CI: 1.9, 3.0). Based on the individual patient data and using the British Society of Paediatric Endocrinology and Diabetes guidelines, the cost analysis shows that for this cohort, the average cost for an episode of DKA was £1387 [95% confidence interval (CI): £1120, £1653]. Regression analysis showed a significant cost saving of £762 [£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 DKA in adolescents. These data suggest that following treatment guidelines can significantly lower the costs for managing episodes of DKA.

Keywords: Diabetic ketoacidosis; adolescents; management; survey, costs, economic

Introduction

Diabetic ketoacidosis (DKA) is a frequently encountered metabolic emergency in adolescents with type 1 diabetes [1]. Recent work has shown that each episode of DKA in an adult in the UK in 2014 cost the National Health Service £2064 per person (95% 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 old [3]. This survey looked at outcomes of a convenience sample of young people with diabetes aged <18 years old (mean age 14.9 years, range 11 - 18) presenting with DKA over a 7 month period. 56 out 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 of these individuals have been described previously [3]. We used this dataset to conduct an analysis 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, and informed by the 2013 British Society of Paediatric Endocrinology and Diabetes (BSPED) guidelines [4]. This is the version of the guideline 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 the resolution of DKA per diem ward costs were used. We used the questionnaires to estimate the quantity of diagnostic tests, as well as time from admission to DKA resolution and time to discharge. The times taken by healthcare 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 minutes by a junior doctor.
- On admission, a nurse took 15 minutes to collect the urine and blood samples.
- Everyone received intravenous insulin according to BSPED guidelines every hour from admission to DKA resolution. This required 5 minutes of junior doctor time and 15 minutes of nurse time per hour.
- For dosing purposes, individuals were assumed to weigh an average of 55kg – the mean weight at the 50^{th} centile of boys (56kg) and girls (54kg) aged 14.9 years [5].
- It took 30 minutes 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 individuals were transferred to a general paediatric ward when their DKA had resolved 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.

- 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 hours 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 [6,7].
- We assumed 30 minutes of nurse time for a follow-up visit from the paediatric specialist diabetes team.

A bottom up costing approach involves resource utilisation at the patient or individual level. The patient level utilisation data are aggregated to identify types of resources used in order to calculate overall costs. In contrast to bottom up approach, top down costing first calculates the total costs of the service at the organisational, provider or departmental level and then disaggregates the total costs to the department or the units of service or products [8].

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 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 (MCAR) [2]. This was because a number of variables had a high proportion of missing values. We performed predictive mean matching (PMM) using the Multivariate Imputation by Chained Equations Package in R statistical software (version 3.4.2) [9]. 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 [10]. The regression model is used to estimate the similarity of the record with other non-missing observations rather than the missing value itself. Table 3 in the online supplementary material shows a summary of the questionnaire data as well as the variables with imputed values. Table 4 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 sub-totals 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 values. A comparison of the observed and imputed total costs is shown in Figure 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 (LOS). 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 the following minimum times that would be spent by induvial members of the clinical staff. A full list of clinical staff, their allocated time, and any procedures and is provided in Appendix 1 in the on line supplementary material. This was constructed by the two authors (VD and PH) using the BSPED DKA guideline [4].

Similarly, we determined the hourly wage rages 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 only considered 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 the account and other factors, such as comorbidities or individual circumstance. 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% confidence interval (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 15.0hrs (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 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 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 6.8h (p=0.001). Resolution time also increased with year of diagnosis, by 0.5h per year (p=0.01). An episode of hypoglycemia 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 Figure 3 in the supplementary materials.

Transfer to HDU

Using the BSPED guidelines, we determined the number of individuals who should have been transferred to an HDU. By 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 an High Dependency Unit (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 (87%) of individuals provided information on their precipitating factors. Of those, 32 (52%) were had poor concordance with their diabetes treatment; seven (11%) had issues with insulin pump or device failures; and 23 (37%) were due a combination of other acute and non-acute illnesses. The granularity of these individual patient level data are what has differentiated the present work from previous studies.

Discussion

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

We acknowledge that the data collected as part of the 2014 national survey were not specifically collected for to allow for detailed health economic analyses. However we were able to use the 2013 BSPED DKA guideline to identify a treatment pathway which 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 as 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 has been done 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 [11,12]. Recent data has suggested that – in the UK – that the rate of DKA has 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 [13]. Most episodes occur in children known to have diabetes during or after transition from the adolescent to the adult service [13,14].

Costs vary with data from the US in 2004 to 2014 estimating that the numbers of admission in the US rose by 62%, and the costs per episode of DKA had also risen from $18,987 (£15,112) to $26,566 (£20,178) [15]. However, these were costs for all DKA admissions. Costs for children – as with the UK data – have been calculated as lower than adults at between $7,429 (£5,642) and $10,881 (£8,264) [16]. Data from Germany did not give estimates of cost per episode, but showed that annual costs of care for individuals who had episodes of DKA were increased compared to those who did not – cost ratio of 2.2 (95%CI 2.1-2.3) for those with just 1 episode of DKA, and 3.6 (95%CI 3.1-4.1) for those with more than one [12].

Cost of DKA

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 saved a potential £1000-1400 – a figure derived from NHS England's guide to the enhanced tariff option for 2015–16 [17]. Our data are consistent with this. One of the main reasons why the average costs for the adolescent DKA population were lower than a similar analysis done for the adult population (£1387 vs £2064), is possibly the length of stay [2]. The median [interquartile range (IQR)] length of stay for adolescents was 1.85 (1.00, 2.74) days, with a mean (SD) of 2.35 (2.3) days, and in the adults, it was 2.0 (1.12, 2.67) days, with a mean (SD) of 2.53 (2.4) days. Whilst this was not statistically significant ($P = 0.3$), a difference in median length of stay of 12 hours 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 intensive care unit, compared to 12.5% of the adult population [3,18]. Not transferring these individuals could have resulted in a lower cost of DKA treatment. Among other plausible reasons, the most significant factor to consider on this aspect would be shortage or unavailability of beds. As a result, institutional arrangement and capacity constraints could have been the influential factors while 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 guideline minimises the room for errors, and determines the 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 [19].

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 [20]. 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 individual patients prior to admission.

Productivity losses

By using forecasts of the population of people 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 [21]. This is given as 195.4 per 100,000 of the general population in those aged 0-15 [21]. 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 [13]. 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 the years to come. What is not taken into account by these data is the loss of productivity of the caregivers / parents whilst 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 treatments of co-morbidities – because these were so disparate and because the sample size was too small to make generalised 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 [12,22]. However, the major strengths of our data are that it was collected from across the UK, and that data 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). Whilst 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.

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Legends to Tables, Figure and Appendices

Table 1 - Cost components - unit prices

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

Figure 1 - Comparison of the observed and imputed total costs

Figure 2 – A Log-normal distribution best fit the imputed total costs

Online supplementary data

Table 3 – Data collection with percentage of missing data and imputed data

Table 4 – Costs by component

Figure 3 – The differences in costs for the BSPED vs non-BSPED groups

Appendix 1 - A full list of allocated time, procedure and clinical staff needed to treat an episode of DKA

Table 1

Cost Component	Unit Cost (£)
Hospital facilities	
Level 1: General Ward – per day	428.49*
Level 2: HDU – per day	889.14*
Level 3: ITU – per day	2004.45*
Acute Medical Unit (AMU) - per day	428.49*
A&E – per day	2552.00*
Other wards – per day	428.49*
Variable	
Healthcare staff (per hour)	
Staff Nurse (Band 6)	13.32**
Specialist Registrar (Middle band)	23.76Ƭ
Junior Doctor	14.39Ƭ
Diabetes Specialist Nurse (Band 6)	16.70**
Variable	
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 Reference [6], ** Data taken from Reference [23], Ƭ Data taken from [24], § Data taken from [25], ¥ Data taken from [26], ∞ Data taken from [27], ¶ Data taken from [28]

Table 2

Treatment Area Distribution (%)	Follow BSPED (n=60)	Don't follow BSPED (n=11)
High Dependency Unit	47	27
General ward	22	18
Accident & Emergency	22	0
Assumption made	0	45*
Acute Medical Unit	5	9
Intensive Care Unit	3	0
Other	2	0
* assumption made for 5 cases here which reported treatment in HDU, AMU or ITU along with A&E.		
Total costs (mean) [95% CI]	£1294 [1065, 1523]	£2151 [869, 3432]
Mean difference		
95 percent confidence interval	£140, £1574	