DIABETICMedicine

DOI: 10.1111/dme.13427

Research: Health Economics

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

K. K. Dhatariya[1], C. Skedgel[2] and R. Fordham[2]

[1]Elsie Bertram Diabetes Centre, Norfolk and Norwich University Hospitals NHS Foundation Trust and [2]Health Economics Consulting, Norwich Medical School, University of East Anglia, Norwich, UK

Accepted 17 July 2017

Abstract

Aim Diabetic ketoacidosis is a commonly encountered metabolic emergency. In 2014, a national survey was conducted looking at the management of diabetic ketoacidosis in adult patients across the UK. The survey reported the clinical management of individual patients as well as institutional factors that teams felt were important in helping to deliver that care. However, the costs of treating diabetic ketoacidosis were not reported.

Methods We used a 'bottom up' approach to cost analysis to determine the total expense associated with treating diabetic ketoacidosis in a mixed population sample. The data were derived from the source data from the national UK survey of 283 individual patients collected via questionnaires sent to hospitals across the country.

Results Because the initial survey collection tool was not designed with a health economic model in mind, several assumptions were made when analysing the data. The mean and median time in hospital was 5.6 and 2.7 days respectively. Based on the individual patient data and using the Joint British Diabetes Societies Inpatient Care Group guidelines, the cost analysis shows that for this cohort, the average cost for an episode of diabetic ketoacidosis was £2064 per patient (95% confidence intervals: 1800, 2563).

Conclusion Despite relatively short stays in hospital, costs for managing episodes of diabetic ketoacidosis in adults were relatively high. Assumptions made in the calculations did not consider prolonged hospital stay due to comorbidities or costs incurred as a loss of productivity. Therefore, the actual costs to the healthcare system and society in general are likely to be substantially higher.

Diabet. Med. 34, 1361–1366 (2017)

Introduction

Diabetic ketoacidosis is one of the most commonly encountered metabolic emergencies, but incidence varies geographically. In the UK, the crude 1-year incidence has been reported as 3.6%, equating to 4.8 episodes per 100 patient years [1,2]. In North America, the 1-year incidence is between 1% and 5% of people with Type 1 diabetes [3,4], equating to ~ 145 000 cases per year [5]. In the Western Pacific region, the rate among children is 10 per 100 patient years [6], but the value is much lower in some parts of Northern Europe [7,8]. Most cases of diabetic ketoacidosis occur in Type 1 diabetes, but up to 50% of cases in some regions occur in those with Type 2 diabetes, depending on ethnicity and family history [9,10]. However, those with Type 1 diabetes tend to have the greatest metabolic derangement, with a lower pH compared with those with Type 2 diabetes [11]. Although there are few datasets, diabetic ketoacidosis remains an expensive condition to treat, with individual admissions estimated to cost approximately $17 500 in the USA. Very little work on how much an episode of diabetic ketoacidosis costs the health service has been carried out until recently in the UK, and the data that have been produced have relied on relatively crude methods.

In 2014, a national survey was carried out in the UK looking at the management of diabetic ketoacidosis. Briefly, this survey consisted of two parts, one looking at outcomes of a convenience sample of up to five consecutive patients presenting with diabetic ketoacidosis over a 7-month period. Some 72 of 220 UK hospitals returned data on 283 admissions in 281 patients, looking at all aspects of their care during the acute hospital admission [12]. The demographic data of these patients have been described previously [12]. In addition, 67 hospitals returned questionnaires on the institutional factors that assessed their ability to provide comprehensive care for adult patients presenting with

Correspondence to: Ketan Dhatariya. E-mail: ketan.dhatariya@nnuh.nhs.uk

What's new?

- Diabetic ketoacidosis is a commonly encountered metabolic emergency, but the costs of treating the condition remain unknown in the UK.
- Using individual patient data from the 2014 national survey we conducted a 'bottom-up' approach to cost analysis.
- The average cost of an episode of diabetic ketoacidosis in the UK in 2014 was £2064 per patient (95% confidence intervals: 1800, 2563).

diabetic ketoacidosis [13]. We used these datasets to conduct an analysis to assess how much it cost to treat diabetic ketoacidosis in adults in the UK in 2014.

Methods

The cost analysis was based on an aggregation of individual-level factors collected as part of the questionnaire, and informed by the Joint British Diabetes Societies (JBDS) Inpatient Care Group guidelines [14]. The key components of our estimate of cost included diagnostic and laboratory assessments, nurse and physician contacts, and drug dosages during the acute diabetic ketoacidosis phase of the admission, and per diem ward costs following the resolution of diabetic ketoacidosis. The quantity of diagnostic tests was recorded in the questionnaire, along with time from admission to diabetic ketoacidosis resolution and time to discharge. Healthcare staff times were based on expert opinion. Our key costing assumptions are detailed below, and unit prices are shown in Table 1.

- Each patient was assessed for 15 min by a junior doctor upon admission.
- Blood and urine samples were collected at admission and required 15 min of nurse time.
- All patients received intravenous insulin according to JBDS guidelines every hour from admission to diabetic ketoacidosis resolution. This required 15 min of nurse time and 5 min of junior doctor time per hour.
- For dosing purposes, patients were assumed to weigh an average of 70 kg.
- Assessment by members of the diabetes specialist team took 30 min of nurse time.
- Location of care during the diabetic ketoacidosis phase was recorded in the questionnaire (see Table 2) and we assumed that patients were transferred to a general ward upon diabetic ketoacidosis resolution for the remainder of their inpatient stay.

Table 1 Cost components – unit prices

Cost component	Unit cost (£)	Ref
Hospital facilities		
Level 1: General ward (per day)	428.49	15
Level 2: High dependency unit (per day)	889.14	15
Level 3: Intensive care unit (per day)	2004.45	15
Acute medical unit (per day)	428.49	15
Accident & Emergency (per day)	2552.00	15
Other wards (per day)	428.49	15
Healthcare staff (per hour)		
Staff nurse (Band 6)	13.32	17
Specialist registrar (middle band)	23.76	18
Junior doctor	14.39	18
Diabetes specialist nurse (Band 6)	16.70	17
Investigations		
X-ray	25.00	19
Laboratory blood tests	1.00	19
Electrocardiogram	32.00	19
Urine test strip	0.43	20
Intravenous insulin	5.24	21
1 L 0.9% sodium chloride solution with potassium	2.20	22

Table 2 Patient distribution by treatment area

Treatment area	Distribution (%)
General ward	16
High dependency unit	14
Intensive care unit	10
Acute medical unit	39
Accident & Emergency	10
Other	2
Assumption made	9

- Where more than one treatment location was recorded in the questionnaire (9% of responses), we assumed that treatment occurred in the more intensive location.
- For patients treated in Accident & Emergency (A&E), we assumed a maximum time of 4 h (as per government targets) after which they were equally likely to be transferred to a high dependency unit (HDU) or intensive care unit (ITU) until resolution of diabetic ketoacidosis.
- Time on the acute wards was costed according to published per diems, and time in the general ward was costed at the best practice tariff for extended days following diabetic ketoacidosis [15,16].
- A follow-up visit from the specialist diabetes team was costed as requiring 30 min of nurse time.

Total costs were estimated as the sum of individual components. Specifically, total cost included the costs of an initial physician assessment, nursing time and diagnostic/laboratory tests, insulin and other drugs during the acute diabetic ketoacidosis phase, ward per diems during active

treatment, and recovery (post diabetic ketoacidosis), as well as a follow-up visit post admission if recorded. We did not include costs associated with any follow-up beyond an initial visit from a member of the diabetes specialist team, or the consequences of any precipitating factors, treating comorbidities, or on the cost of diabetes to society in general.

Missing data and imputation

A summary of the questionnaire data is shown in Table S1. Because several variables had a high proportion of missing values, we used multiple imputation methods to infer values for missing values, assuming values were missing completely at random (MCAR). We performed predictive mean matching (PMM) using the Multivariate Imputation by Chained Equations Package in R statistical software (version 3.3.2) [23]. Briefly, PMM 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 [24]. 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 the variables with imputed values. Table S2 lists the costs by individual component. We did not impute non-continuous variables such as flags indicating a particular blood test or imaging procedure. Instead, we imputed the continuously distributed subtotals for the individual components noted above (physician assessment, nursing time, diagnostic/laboratory tests, insulin and other drugs, ward per diems), and used the sum of these components to estimate total cost. This allowed the estimated total cost to be based on observed values as much as possible while avoiding strong assumptions about the distribution of non-normal parameters. A comparison of the observed and imputed total costs is shown in Fig. 1.

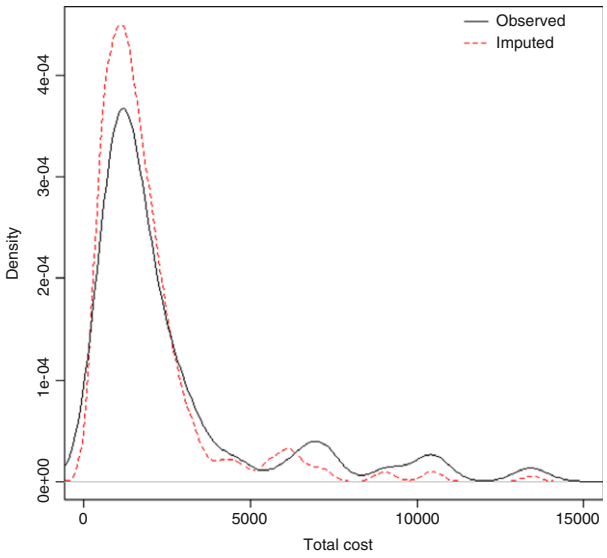

FIGURE 1 Comparison of the observed and imputed total costs.

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 age, gender, the number of previous diabetic ketoacidosis admissions, and flags indicating hypoglycaemia following resolution of diabetic ketoacidosis and whether diabetic ketoacidosis treatment followed JBDS guidelines.

Clinical care staff

To determine the amount of time spent by clinical care staff such as nurses and doctors in managing the patients, we sought expert opinion from a consultant in diabetes medicine. We determined the following minimum times that would be spent by clinical staff. A full list of allocated time, procedure and clinical staff is provided in Appendix S1. This was constructed by a one of the authors (K.D.) using the JBDS diabetic ketoacidosis guidelines [25].

Similarly, to be able to determine the costs associated with clinical care staff time we determined the hourly wage rages of a range of different staff. Sources of salaries and other costs are provided in Table 1.

Costs of diabetic ketoacidosis were only considered from a hospital perspective and the admission of the patient to the resolution of diabetic ketoacidosis. However, cost analysis was done for the duration of diabetic ketoacidosis treatment and not the whole duration of the patient's stay to provide an accurate picture of the impact of diabetic ketoacidosis and the associated costs with patient treatment. This allows us to determine the impact of diabetic ketoacidosis on the National Health Service (NHS), but does not take into the account patient circumstance or comorbidities. These circumstances could be medical or social and many cases led to lengthier hospital stays and subsequently higher costs than would be the case of diabetic ketoacidosis alone.

Results

The mean cost per episode of diabetic ketoacidosis was £2064 per patient [95% confidence interval (CI): 1800, 2563], including physician and nursing time, laboratory and diagnostic assessments, intravenous insulin, and ward per diems. The mean time to diabetic ketoacidosis resolution was 22.3 h (95% CI: 20.3, 24.3) and the mean total length of stay was 5.6 days (95% CI: 3.9, 7.2).

We found that a theoretical log-normal distribution, with a log mean of 7.206 and standard error of 0.05, had the best fit

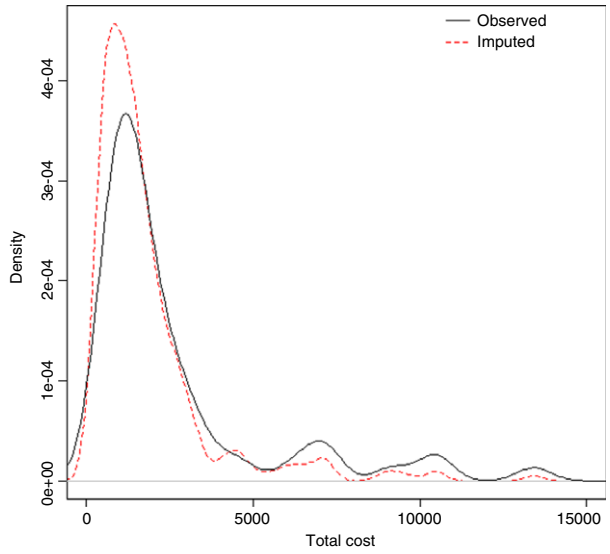

FIGURE 2 Log-normal distribution best fit the imputed total costs.

with the observed (imputed) distribution of total costs (BIC 4791.8) compared with a gamma distribution (BIC 5031.8). The empirical and theoretical distributions are shown in Fig. 2.

The distribution of patients by treatment area is shown in Table 2. A majority of patients were treated in acute medical units and general wards, with only one-third treated in higher intensity areas.

Predictors of cost and length of stay

An episode of hypoglycaemia following diabetic ketoacidosis had a statistically significant impact, reducing the mean cost of an event by £935 ($P = 0.03$). Males had a significantly shorter time to diabetic ketoacidosis resolution (–6.2 h, $P = 0.003$). The other parameters were not statistically significant at 5%.

Transfer to HDU

Initially, according to the guidelines, we determined the number of patients who should have been transferred to an HDU. By observing three important factors (bicarbonate concentration, pH and potassium concentration) we determined that, according to the JBDS guidelines, 35% of the patients should have been treated in an HDU or ITU. However, only 4% of patients were actually treated in these areas. Not transferring these patients would most likely have resulted in higher cost for diabetic ketoacidosis treatment. A range of plausible reasons might influence whether the patient was moved to an HDU or ITU, the most significant being a shortage or unavailability of beds [26]. Hence, costs may have been influenced by institutional arrangements and capacity constraints.

Hypoglycaemia

Another factor that might impact on the length of stay was whether the patient had an episode of hypoglycaemia after their diabetic ketoacidosis treatment. Twenty-eight per cent of patients in our cohort had a hypoglycaemic episode. Somewhat surprisingly, however, our data showed that an episode of hypoglycaemia was associated with a significant reduction in costs, by £935. These data contradict previous work showing that hypoglycaemia is associated with a longer length of stay and increased mortality [27]. We are unable to explain this difference and clearly this is an area where more work needs to be done.

Cost impact of precipitating causes

As part of the analysis we also looked at precipitating factors that were associated with diabetic ketoacidosis. The nationally collected data used in this analysis showed that 77% of patients provided information on their precipitating factors. Of those, 21% of patients were not complying with their diabetes treatment, 5% had new-onset diabetes and the remaining 51% of diabetic ketoacidosis cases were due a combination of other acute and non-acute illnesses. These data differentiated the this work from previous studies because of the granularity of the information that was obtained from individual patient level data.

Discussion

This study has shown that in 2014, the average cost of treating an episode of diabetic ketoacidosis in an adult patient in the UK was £2064 (95% CI: 1800, 2563).

The data collected as part of the national survey were not specifically collected for health economic analysis. However, we were able to identify a treatment pathway based on the JBDS diabetic ketoacidosis guidelines that was used by the majority of hospitals who returned data. We were also able to determine the staff type and time required in each treatment step, as well as being able to determine the impact of a range of physiological results upon the resolution of diabetic ketoacidosis. This allowed us to determine the cost associated with the treatment of diabetic ketoacidosis in a more granular fashion than has been done previously. However, the costs identified in this study do not account for hospital overheads, which are often included in Healthcare Resource Groups codes and their associated cost calculation per event. Healthcare Resource Groups codes are groups of clinically similar treatments which use similar quantities of resource [28].

Cost of diabetic ketoacidosis

Direct healthcare costs

The current study is one of the first to present the costs of diabetic ketoacidosis from a secondary care perspective. A

previous study involved requesting data from primary care organizations on the costs associated with diabetic ketoacidosis admissions [29]. The authors stated that only 32% of the primary care organizations provided such information which showed that the average total cost of diabetic ketoacidosis was £1438 per patient. The report also stated median overall cost of treating diabetic ketoacidosis among the primary care organizations was £125 440 [29]. A more recent study (presented in abstract form only) reported data from a high-risk subpopulation of individuals who suffered from recurrent diabetic ketoacidosis events over a retrospective 3-year period [30]. The resultant cost analysis of the data from that single centre study showed that the average cost per patient per year was £1803.

Productivity losses

Previous work on the costs associated due to lost productivity in people with Type 1 diabetes estimated that 37 000 work years are lost due to premature death [31]. Furthermore, they showed that > 830 000 sick days were taken by people with Type 1 diabetes. From the prevalence figures, we can estimate the number of work years lost and time taken off work due to sickness to be ~ 12 000 and 27 000 years respectively. However, no work has been done that looks at the costs associated with productivity loss from diabetic ketoacidosis.

By using forecasts of the population with diabetes increasing over the coming years and data on incidence rates of diabetic ketoacidosis, it is possible to assign values to future costs of diabetic ketoacidosis treatment. This is particularly possible using the crude prevalence rate of Type 1 diabetes mentioned earlier; the crude prevalence rate of diabetic ketoacidosis events in the UK and the predicted yearly increase in the diabetes population. We can multiply this figure by the average patient cost for diabetic ketoacidosis and determine the economic burden of the disease for the years to come.

It may well be that the differences between costs in the UK and the USA are due, in part, to the higher number of people looked after in Level 2 (HDU) or Level 3 (ITU) environments. These are more expensive areas within the hospital. Had more-sick patients been treated in these – more appropriate – clinical environments, then the overall costs would have been higher.

There are several limitations to our study. The data came from a retrospective convenience sample and were not in a form that was easily usable for health economic analysis; many assumptions had to be made. In addition, we did not add on further salary costs (e.g. employers 'on costs') or costs associated with the treatment of comorbidities because these were very disparate. Our sample size was too small to make general assumptions about these comorbidities. In addition, we could not cost for recurrent readmissions because the 283 cases of diabetic ketoacidosis represented 281 individual patients. However, the major strengths of our study are that the data were collected from across the UK, and were available for a large number of patients for all stages of the patient journey from which appropriate calculations could be made.

In summary, treating an episode of diabetic ketoacidosis in an adult patient in the UK in 2014 cost, on average, £2064 (95% CI: 1800, 2563). Many assumptions were made to allow these calculations, but as the number of people with diabetes increases, it is likely that the number admitted with diabetic ketoacidosis will also increase. In addition, given the many assumptions made it is likely that the true costs of an episode of diabetic ketoacidosis are much higher. These data should be used to enable funders to plan for future costs associated with this potentially life-threatening medical emergency.

Funding sources

C.S. and R.F. are employees of the University of East Anglia. K.K.D. is an employee of the UK National Health Service.

Competing interests

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

Acknowledgments

The authors wish to acknowledge the contribution of Bishal Mohindru who made an early contribution to the study and helped collect cost data.

References

1 Health and Social Care Information Centre. National Diabetes Audit 2012–2013. Report 2: complications and mortality. Available at http://www.hscic.gov.uk/catalogue/PUB16496/nati-diab-audi-12-13-rep2.pdf Last accessed 25 May 2017.
2 Karges B, Rosenbauer J, Holterhus PM, Beyer P, Seithe H, Vogel C *et al.* Hospital admission for diabetic ketoacidosis or severe hypoglycemia in 31,330 young patients with type 1 diabetes. *Eur J Endocrinol* 2015; **173**: 341–350.
3 Faich GA, Fishbein HA, Ellis SE. The epidemiology of diabetic acidosis: a population-based study. *Am J Epidemiol* 1983; **117**: 551–558.
4 Ginde AA, Pelletier AJ, Camargo CA. National study of U.S. emergency department visits with diabetic ketoacidosis, 1993–2003. *Diabetes Care* 2006; **29**: 2117–2119.
5 Centers for Disease Control and Prevention. Number (in thousands) of hospital discharges with diabetic ketoacidosis (DKA) as first-listed diagnosis, United States, 1988–2009. Available at http://www.cdc.gov/diabetes/statistics/dkafirst/fig1.htm Last accessed 25 May 2017.
6 Craig ME, Jones TW, Silink M, Ping YJ. Diabetes care, glycemic control, and complications in children with type 1 diabetes from Asia and the Western Pacific Region. *J Diabetes Complicat* 2016; **21**: 280–287.
7 Henriksen OM, Roder ME, Prahl JB, Svendsen OL. Diabetic ketoacidosis in Denmark. *Diabetes Res Clin Pract* 2007; **76**: 51–56.

8 Rosilio M, Cotton JB, Wieliczko MC, Gendrault B, Carel JC, Couvaras O *et al*. Factors associated with glycemic control: a cross-sectional nationwide study in 2,579 French children with type 1 diabetes. *Diabetes Care* 1998; **21**: 1146–1153.
9 Wang ZH, Kihl-Selstam E, Eriksson JW. Ketoacidosis occurs in both Type 1 and Type 2 diabetes – a population-based study from Northern Sweden. *Diabet Med* 2008; **25**: 867–870.
10 Umpierrez GE, Smiley D, Kitabchi AE. Narrative review: ketosis-prone type 2 diabetes mellitus. *Ann Intern Med* 2006; **144**: 350–357.
11 Newton CA, Raskin P. Diabetic ketoacidosis in type 1 and type 2 diabetes mellitus: Clinical and biochemical differences. *Arch Intern Med* 2004; **164**: 1925–1931.
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. *Diabet Med* 2016; **33**: 252–260.
13 Dhatariya K, Nunney I, Iceton G. Institutional factors in the management of adults with diabetic ketoacidosis in the UK: results of a national survey. *Diabet Med* 2016; **33**: 269–270.
14 Dhatariya K, Savage M, Kelly T, Sampson M, Walden E *et al*.; Joint British Diabetes Societies Inpatient Care Group. The management of diabetic ketoacidosis in adults. Second edition. Updated September 2013. Available at http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm Last accessed 25 May 2017.
15 Welsh Government. Together for Health – a delivery plan for the critically ill. A delivery plan up to 2016 for NHS. The highest standard of care for everyone who is critically ill. Available at http://www.wales.nhs.uk/documents/delivery-plan-for-the-critically-ill.pdf Last accessed 25 May 2017.
16 NHS Improvement, NHS England. 2017/18 and 2018/19 National Tariff: currencies and prices. Available at https://improvement.nhs.uk/uploads/documents/Copy_of_Annex_A_-_National_tariff_workbook.xlsx Last accessed 25 May 2017.
17 National Institute for Health and Clinical Excellence. NICE cost impact and commissioning assessment for diabetes in adults. Available at https://www.nice.org.uk/guidance/qs6/resources/cost-impact-and-commissioning-assessment-for-diabetes-in-adults-252278029 Last accessed 25 May 2017.
18 NHS Employers. Pay and conditions circular (M&D) 1/2016. Available at http://www.nhsemployers.org/~/media/Employers/Documents/Need%20to%20know/Pay%20Circular%20MD%201%20%202016%20general%20uplift%20finaldoc.pdf Last accessed 25 May 2017.
19 Department of Health. NHS reference costs collection guidance for 2014 to 2015. Available at https://www.gov.uk/government/publications/nhs-reference-costs-collection-guidance-for-2014-to-2015 Last accessed 25 May 2017.
20 Medisupplies. Bayer multistix diagnostic supplies. Available at https://www.medisupplies.co.uk/Diagnostic-Equipment/Blood-Urinalysis-Testing/Urinalysis-Testing/Bayer-Multistix-Diagnostic-Strips Last accessed 25 May 2017.
21 British Medical Association, Royal Pharmaceutical Society of Great Britain. *British National Formulary*. London: Authors, 2017.
22 MedicinesComplete. Potassium chloride with sodium chloride. Available at https://www.medicinescomplete.com/mc/bnf/current/PHP87990-potassium-chloride-with-sodium-chloride.htm?q=Potassium&t=search&ss=text&tot=543&p=6#_hit Last accessed 25 May 2017.
23 van Buuren S, Groothuis-Oudshoorn K. Multivariate imputation by chained equations in R. *J Stat Softw* 2011; **45**: 1–67.
24 Morris TP, White IR, Royston P. Tuning multiple imputation by predictive mean matching and local residual draws. *BMC Med Res Methodol* 2014; **14**: 75.
25 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. *Diabet Med* 2011; **28**: 508–515.
26 Fletcher S. The critical care/acute medicine interphase. *Future Hosp J* 2016; **3**: 55–57.
27 Nirantharakumar K, Marshall T, Kennedy A, Hemming K, Coleman JJ. Hypoglycaemia is associated with increased length of stay and mortality in people with diabetes who are hospitalized. *Diabet Med* 2012; **29**: e445–e448.
28 NHS Digital. Introduction to Healthcare Resource Groups. Available from http://content.digital.nhs.uk/hrg Last accessed 19 April 2017.
29 Allan J, Howarth S. Diabetes and DKA in England's Primary Care Trusts. Available at http://dwed.org.uk/s/DwedReportDKAPCT.pdf Last accessed 25 May 2017.
30 Byrne ML, Mills LS, Saunders S, Garrett CJ. The economic burden and mortality of recurrent diabetic ketoacidosis: a 3 year cost analysis and mortality follow-up at a district general hospital. Poster 496. Available at https://doi.org/onlinelibrary.wiley.com/doi/10.1111/dme.51_13048/epdf Last accessed 25 July 2017.
31 Hex N, Bartlett C, Wright D, Taylor M, Varley D. Estimating the current and future costs of Type 1 and Type 2 diabetes in the United Kingdom, including direct health costs and indirect societal and productivity costs. *Diabet Med* 2012; **29**: 855–862.

Supporting Information

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

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.