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A retrospective observational study of people with Type 1 diabetes with self-reported severe hypoglycaemia reveals high level of ambulance attendance but low levels of therapy change and specialist intervention

Short running title: Limited interventions after self-reported severe hypoglycaemia in Type 1 DM

Authors: BCT Field¹,²*, R Nayar³*, A Kilvert⁴, M Baxter⁵, J Hickey⁶, M Cummings⁷, SC Bain⁸

*BCT Field and R Nayar should be considered joint first author

Author affiliations:

¹Endocrinology and Diabetes, East Surrey Hospital, Surrey & Sussex Healthcare NHS Trust, Redhill, UK.

²Section of Investigative Medicine, Imperial College London, London, UK.

³Endocrinology, Sunderland Royal Hospital, City Hospitals Sunderland NHS Foundation Trust, Sunderland, UK.

⁴Diabetes Centre, Northampton General Hospital, Northampton NHS Trust, Northampton, UK.

⁵Medical Affairs - Diabetes, Sanofi, Guildford, UK.

⁶pH Associates, The Weighbridge, High Street, Marlow, UK.

⁷Diabetes Centre, Queen Alexandra Hospital, Portsmouth NHS Trust, Portsmouth, UK.

⁸Diabetes Research Unit Cymru, Swansea University Medical School, Swansea, UK.
Corresponding author:

Professor Stephen C Bain

E-mail: s.c.bain@swansea.ac.uk

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Conflicts of Interest

BCTF has no conflicts to declare; RN has received personal fees and other support from Sanofi, personal fees and non-financial support from Eli Lilly, grants, personal fees and other support from Novo Nordisk, personal fees from MSD, personal fees from Janssen and personal fees from Astra Zeneca; AK has no conflicts to declare; MB is an employee of Sanofi; JH is an employee of pH associates; MC has received speaker honorarium from Sanofi; SCB has received grants and personal fees from Sanofi, grants and personal fees from Eli Lilly, grants and personal fees from Boehringer Ingelheim, grants and personal fees from Astra Zeneca, grants and personal fees from Novo Nordisk, grants and personal fees from MSD, grants from GenMedica, grants from CeQur; no other relationships or activities that could appear to have influenced the submitted work.

Novelty Statement

• 71% of episodes of self-reported severe hypoglycaemia involved ambulance call out.
• Only 13% of all diabetes clinic consultations were documented as hypoglycaemia follow-up and at least 50% of people included in this study had no documented healthcare professional-recommended changes to diabetes treatment.

• The results of our study suggest a lack of a consistent mechanism for reporting by paramedics to primary care and subsequent referral to specialist diabetes services, a lack of a consistent approach to early follow-up by specialist diabetes services, and low levels of healthcare professional-recommended therapy change and ongoing specialist review following self-reported episodes of severe hypoglycaemia.

Acknowledgements

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Author Contributions

BCTF, RN, AK, SCB were involved in the acquisition, analysis and interpretation of the data, critical revision of the manuscript for important intellectual content and approval of the final version of the manuscript. MB was involved in the analysis and interpretation of the data, critical revision of the manuscript for important intellectual content and approval of the final version of the manuscript. JH was involved in the analysis and interpretation of the data, drafting of the manuscript and approval of the final version of the manuscript. MC was involved in the acquisition and interpretation of the data, critical revision of the manuscript for important intellectual content and approval of the final version of the manuscript. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data Sharing Statement

Data sharing: no additional data available.
Abstract

Aims. To evaluate the impact of severe hypoglycaemia on NHS resources and overall glycaemic control in adults with Type 1 diabetes.

Methods. An observational, retrospective study of adults (aged ≥18 years) with Type 1 diabetes reporting one or more episodes of severe hypoglycaemia during the preceding 24 months in 10 NHS hospital diabetes centres in England and Wales. The primary outcome was healthcare resource utilisation associated with severe hypoglycaemia. Secondary outcomes included demographic and clinical characteristics, diabetes control and pathway of care.

Results. 140 episodes of severe hypoglycaemia were reported by 85 participants during the 2-year observation period. Ambulances were called in 99/140 (71%) episodes, Accident and Emergency attendance occurred in 26/140 (19%) episodes, whereas 29/140 (21%) required no immediate help from healthcare providers. Participants attended a median of 5 (range: 0–58) diabetes clinic consultations during the observation period; 13% (70/552) of all consultations were severe hypoglycaemia-related. Of the HbA1c measurements recorded closest prior to severe hypoglycaemia (n=119), only 7/119 measurements were <48 mmol/mol (<6.5%) and mean HbA1c was 70 (SD: 19) mmol/mol (8.5% [SD: 1.7%]). 119 changes to diabetes treatment were recorded during the observation period (median/person 0 [range: 0–11]), of which 52/119 changes (44%) followed severe hypoglycaemic events.

Conclusions. We observed a high level of ambulance service intervention but surprisingly low levels of hypoglycaemia follow-up, therapy change and specialist intervention in people
self-reporting severe hypoglycaemia. These results suggest there may be important gaps in care pathways for people with Type 1 diabetes self-reporting severe hypoglycaemia.

**Related conference abstracts**


**Keywords**

Retrospective, Type 1 diabetes, hypoglycaemia, HbA1c, health resources, ambulance
Introduction

Persistent hyperglycaemia in Type 1 diabetes is associated with microvascular complications and an increased risk of cardiovascular disease [1]. The Diabetes Control and Complications Trial (DCCT) demonstrated that intensive glycaemic control significantly reduced the incidence of microvascular and cardiovascular disease and slowed progression of microvascular complications [1–3]. However, intensive glycaemic control is associated with an increased risk of severe hypoglycaemia, defined as an event requiring the assistance of another person to treat [1,4].

Severe hypoglycaemia is associated with an increased risk of cardiovascular events [5], a reduction in quality of life, increased fear and anxiety, reduced productivity, and increased healthcare costs [4]. Fear of hypoglycaemia can lead to complex compensatory behaviour resulting in sub-optimal glycaemic control and an increased risk of developing chronic complications [4,6]. Modern Type 1 diabetes management emphasises structured education, for example through the DAFNE (Dose Adjustment for Normal Eating) programme [7], to enable people to tailor insulin dosing according to carbohydrate intake and exercise [4,8]. Despite such developments, severe hypoglycaemia remains a major hazard for people with Type 1 diabetes and is the most common diabetes emergency requiring ambulance service call-out and Accident and Emergency (A&E) attendance [9,10].

Although studies have reported resource utilisation associated with severe hypoglycaemia requiring ambulance attendance [5,9,11–14], there is limited real-world evidence reporting secondary care resource utilisation and clinical intervention specifically associated with episodes of self-reported severe hypoglycaemia in people with Type 1 diabetes.
The objective of this study was to evaluate the impact of self-reported episodes of severe hypoglycaemia on secondary care resource use and diabetes management in people with Type 1 diabetes in a real-world setting, in order to understand current unmet need.
Methods

Study design and setting

We conducted an observational, multi-centre, retrospective study of people with Type 1 diabetes in 10 NHS secondary care diabetes centres in England and Wales. Adults (>18 years of age) with Type 1 diabetes currently under the care of participating centres who had been treated with insulin for ≥2 years and who had experienced ≥1 self-reported episode of severe hypoglycaemia in the previous 24 months were eligible for the study.

Participants

Eligible individuals were identified by members of the study team through a review of recent diabetes clinic lists, medical records and local databases and selected in reverse chronological order. Participants gave written informed consent for data collection from medical records according to a protocol approved by the NHS Research Ethics Service (reference 15/NI/0169). Data were collected between November 2015 and April 2016.

Sample size

As a retrospective descriptive study with a single cohort of participants, no formal power calculation was carried out. A target sample size of 50-80 was chosen to provide a representative sample of people with self-reported episodes of severe hypoglycaemia and provide adequate reliability for the study endpoints.

Variables and outcomes

The primary outcome of the study was a summary of the secondary healthcare resource utilisation associated with management of people with Type 1 diabetes self-reporting ≥1 episodes of severe hypoglycaemia. Healthcare resource utilisation included all diabetes
clinic consultations, planned and unplanned inpatient admissions, and other points of care
in the diabetes pathway, including ambulance call-outs and Accident and Emergency (A&E)
attendances during a 2-year period prior to data collection (observation period). Secondary
outcomes included a summary of the profile of individuals reporting severe hypoglycaemia,
their overall glycaemic control and pathway of care. Participant demographic and clinical
characteristics (data as recorded closest to the time of data collection) included age, sex,
duration of diabetes, body mass index (BMI), HbA1c, insulin therapy, comorbidities and
concomitant medication. Glycaemic control and pathway of care included all documented
episodes of severe hypoglycaemia, HbA1c measurements and insulin therapy changes
recorded during the 2-year observation period. Post-hoc exploratory outcomes included:
level of HbA1c measured closest prior to severe hypoglycaemia; time between episodes of
severe hypoglycaemia and hypoglycaemia follow-up consultations; temporal relationship
between episodes of severe hypoglycaemia, diabetes clinic consultations and changes to
diabetes treatment.

Statistical analyses

Data were analysed with descriptive statistics, using only the available data; denominators
are presented for all analyses where data were missing. Quantitative variables are
presented as median (interquartile range [IQR] and/or range) or arithmetic mean (standard
deviation [SD]). Categorical variables are presented as frequency (%).

Costs associated with hospital resource utilisation were calculated using NHS reference
costs 2014/2015 [15].

Sub-group analysis
In order to examine the temporal relationship between episodes of severe hypoglycaemia, diabetes clinic consultations and changes to diabetes treatment, we evaluated a sub-group of 72 severe hypoglycaemic episodes (in 63 participants) with 3 months’ data available both before (pre-hypo) and after the event (post-hypo).
RESULTS

Baseline participant demographic and clinical characteristics

Eighty-five participants from 10 hospitals in England and Wales were studied. Demographic and clinical characteristics are shown in Fig. 1 and Table 1. The mean age at data collection was 57.0 (SD: 14.8) years, 59% (n=50) of participants were men, and the mean duration of diabetes was 33.1 (SD: 14.2) years. At least one comorbidity was recorded for 78 (92%) participants (mean of 3.9 comorbidities [SD: 2.9] per person); none had Addison’s disease and only one had coeliac disease. The majority were using analogue and/or human sequence insulins, either in a multiple daily injection regimen (MDI) or as a continuous subcutaneous insulin infusion (CSII).

Severe hypoglycaemic events and glycaemic control during the 2-year observation period

A total of 140 episodes of severe hypoglycaemia were recorded during the 2-year observation period (median episodes per person 1 [range: 1–4]); 35/85 (41%) participants experienced more than one episode (Fig. 2). The majority of episodes required the assistance of a paramedic (106/140 episodes [76%]). Family members provided assistance for 15% (21/140) of episodes.

A mean of 4.3 (SD: 1.9) HbA1c measurements per person (range: 1–10) were recorded during the 2-year observation period; 11/85 participants (13%) had at least one HbA1c concentration of ≤48 mmol/mol (≤6.5%) and 39/85 participants (46%) had at least one HbA1c concentration of ≤58 mmol/mol (≤7.5%) recorded at some point during the 2-year observation period. For the HbA1c recorded most closely prior to episodes of severe
hypoglycaemia (n=119 measurements; median time prior to hypoglycaemic episode 104 [range: 0–542] days), only 7/119 (6%) measurements were <48 mmol/mol (<6.5%), and the mean HbA1c concentration was 70 (SD: 19) mmol/mol (8.5% [SD: 1.7%]; Fig. 3).

Healthcare resource utilisation

**Severe hypoglycaemic event-related resource utilisation**

Ninety-nine of 140 episodes of severe hypoglycaemia (71%) involved ambulance call-outs (Table 2), of which 83 required no onward emergency care. Sixteen call-outs led to A&E attendance, of which 5 led to non-elective inpatient admission. Ten episodes (7%) involved A&E visits without ambulance call-out or admission, 2 (1%) episodes involved other hospital interventions and 29 (21%) episodes were managed without immediate healthcare professional (HCP) intervention (Table 2). The mean cost of the early management of severe hypoglycaemia during the 2-year observation period was £240.52 per episode (Table 2). Ambulance call-out costs alone (£18,668) accounted for 55.4% of the total severe hypoglycaemia-related healthcare expenditure.

**Diabetes clinic consultations during the 2-year observation period**

During the 2-year observation period, participants attended a median of 5 (IQR: 2–7; range: 0–58) diabetes clinic consultations (Table 3). Only 70/552 (13%) consultations were recorded as for hypoglycaemia follow-up (in 48 participants); of these, 10/70 (14%) did not follow a reported episode. The median time between episodes of severe hypoglycaemia and hypoglycaemia follow-up consultations (n=60) was 2 (range: 0–270) days, with 19/60 (32%) taking place on the same day (telephone consultations; Fig. 2).

**Adjustments to diabetes treatment**
Overall, 119 HCP-recommended adjustments to diabetes treatment were recorded during the 2-year observation period (median per person 0 [range: 0–11]). The most commonly recorded reason for treatment changes was hypoglycaemic event (52/119 changes [44%]; Table 4).

Timing of diabetes clinic visits and anti-diabetes medication adjustments in relation to severe hypoglycaemia

For the sub-group of 72 episodes of severe hypoglycaemia with 3 months’ data available pre- and post-hypoglycaemia, 68 routine diabetes management and 41 hypoglycaemia follow-up consultations were recorded during the 6 month period; of these, 28/109 (26%) occurred during the 3 months before, 12/109 (11%) occurred on the same day (telephone consultations) and 69/109 (63%) occurred during the 3 months after the event. Forty diabetes treatment changes were recorded during this 6-month period; of these, 7/40 (18%) occurred during the 3-months before (median 0 [range: 0–3]; 4/7 changes were dose increases), 4/40 (10%) occurred on the same day (median per person 0 [range: 0–2]) and 29/40 (73%) occurred during the 3 months after the episodes of severe hypoglycaemia. Forty-three percent of changes were dose reductions, all of which were recorded in the 3 months following episodes of severe hypoglycaemia.

Non-hypoglycaemia-related NHS resource utilisation

Overall, 118 non-hypoglycaemia-related hospital attendances/admissions were recorded during the 2-year observation period, including 45 non-elective admissions (Figure S1).
Discussion

Despite the association between intensive/tight glycaemic control and the increased risk of hypoglycaemia reported in the DCCT [1,4], the large majority of participants with self-reported severe hypoglycaemia in our study had relatively poor glycaemic control. Two-fifths of participants had more than one episode of severe hypoglycaemia during the 2-year observation period and almost three-quarters of all episodes involved an ambulance call-out. Despite this, the frequency of diabetes clinic consultations and HbA$_1c$ assessments was lower than expected. Only 13% of consultations were documented as being for hypoglycaemia follow-up and at least 50% of participants did not have any HCP-recommended changes to diabetes treatment documented during the 2-year observation period.

The frequency of severe hypoglycaemia observed in our study is consistent with the prevalence estimated in people with Type 1 diabetes from real-world studies of between 0.7 to 1.59 events per person per year, although considerably higher than the prevalence reported in clinical trials (0.15 to 0.5 episodes per person per year) [16]. We also found that 71% of all hypoglycaemic episodes involved ambulance call-outs, which is greater than that reported in clinical trials [17]. This may reflect the practice of excluding people with Type 1 diabetes at high risk of severe hypoglycaemia from clinical trials and differences in age and social support between our study population and clinical trial participants.

The majority of participants in our study were treated with MDI insulin analogues, consistent with NICE recommendations for adults with Type 1 diabetes [8]. However, only 11% of participants achieved an HbA$_1c$ at or below the NICE recommended target of 48 mmol/mol (6.5%) at any point during the observation period. These data are consistent with
previous studies including DCCT [1], the National Diabetes Audit (NDA) [18], and results of a recent systematic review and meta-analysis [19], and suggest that the current NICE-recommended HbA1c target remains aspirational and are unachievable for the majority of people. The relatively poor glycaemic control observed in our study is consistent with previous studies demonstrating that severe hypoglycaemia is associated with greater glucose variability and higher HbA1c levels [20,21]. Severe hypoglycaemia is also associated with longer duration of diabetes, impaired hypoglycaemia awareness, cognitive impairment, increased burden of comorbidities, β-blocker use and alcohol use [20–22], suggesting the high burden of comorbidities and concomitant medication use observed in our study may have contributed to the increased risk for developing severe hypoglycaemia.

The ambulance service managed the majority of severe hypoglycaemic episodes without a requirement for A&E or inpatient admission, consistent with results of previous real-world studies [11–14,23,24]. This is likely to reflect UK recommendations for the development of pathways of care to reduce inpatient admissions in people with diabetes, including ‘see and treat’ policies for managing severe hypoglycaemia without admission, where appropriate [10]. Importantly, it is also recommended that collaborative pathways of care link hypoglycaemia-related ambulance attendances with enhanced diabetes education and medication review by patients’ usual diabetes service [10]. Therefore, considering NICE recommends review and HbA1c measurements every 3–6 months for people with uncomplicated Type 1 diabetes [8], the frequency of outpatient review for this high-risk cohort was low. Although two-fifths of participants had more than one episode of severe hypoglycaemia, only 13% of all diabetes clinic visits were recorded as being for hypoglycaemia follow-up. Despite a higher frequency of diabetes clinic consultations for routine diabetes management or hypoglycaemia follow-up in the 3 months after an episode
than before, there is no indication in our study of a sustained increase in frequency of review following severe hypoglycaemia. Furthermore, no changes to diabetes treatment were recorded in >50% of our participants during the 2-year observation period. Therefore, despite considerable innovation in development of effective pathways for automatic ambulance service referral of people with hypoglycaemia to primary, community and secondary care services for early follow-up [12,14,25], our results may suggest that specialist diabetes services are clinically unresponsive to (or remain unaware of) severe hypoglycaemic episodes. However, since individuals routinely self-manage their insulin therapy to balance daily carbohydrate consumption and activity, it is possible that some participants were aware of the cause of hypoglycaemia and took action to avoid future occurrences without requiring healthcare advice.

The rates of admissions for severe hypoglycaemia in individuals with Type 1 diabetes, after adjusting for population prevalence, has fallen in recent years; however, due to the increasing prevalence of diabetes, treatment of severe hypoglycaemia has important implications for healthcare resources [26]. Admissions for severe hypoglycaemia have been estimated to cost the NHS an average of £1034 per event [27]. Our study has estimated that the average cost associated with self-reported episodes of severe hypoglycaemia that are largely managed without hospital admission is £240.52, with the major financial burden being shouldered by the ambulance service. These results are broadly consistent with previous UK studies specifically evaluating severe hypoglycaemia requiring ambulance service attendance [11,14,24]. However, the burden of severe hypoglycaemia is not only financial: there is also a significant effect on individuals in terms of reduced quality of life, reduced work productivity and poorer clinical outcomes [16]. Most importantly, it has been reported that 4.45% of people with Type 1 diabetes with severe hypoglycaemia requiring an
ambulance call-out died within 12 months of the last presentation, with a median age of 54 years [13], and 5.2% of people hospitalised for severe hypoglycaemia died within 30 days in 2010 [28]. In this context, the high level of ambulance service intervention but low levels of hypoglycaemia follow-up, therapy change and specialist intervention observed in our study suggest, firstly, a missed opportunity to reduce future risk of hypoglycaemia and, secondly, a need for greater integration of care pathways for people with Type 1 diabetes and severe hypoglycaemia. The majority of episodes of severe hypoglycaemia evaluated in our study required ambulance service attendance, supporting the prominent role of ambulance services in delivering, deliver, or facilitating access to, healthcare advice and support at a time when people (and carers) may be most receptive [11,12,14,23,24]. However, 21% of episodes in our study did not involve immediate HCP intervention, suggesting that directly questioning people with Type 1 diabetes about episodes of severe hypoglycaemia using standardised clinical scales at every diabetes clinic visit may help to improve reporting, evaluation and intervention for all patients experiencing severe hypoglycaemia.

**Strengths and weaknesses of the study**

Our cohort may not be representative of the wider population of people with Type 1 diabetes suffering severe hypoglycaemia for a number of reasons. The majority of participants included in this study were older than 55 years, broadly consistent with previous observational studies [13,14,24] and suggesting that older people with Type 1 diabetes are more prone to episodes of severe hypoglycaemia [29]. However, younger people with Type 1 diabetes (<40 years) are reported to be less likely to attend diabetes appointments [18] and are less likely to self-report severe hypoglycaemia due to the risk of disqualification from driving [30]. Therefore, younger people may be under-represented in
our cohort and those of previous observational studies. As with all retrospective studies, the interpretation of our results is reliant on the quality of the information available in participants’ medical records. Therefore, as participant identification relied on self-reported severe hypoglycaemia, those episodes requiring no interaction with NHS services could not be verified and are likely to have been under-reported (because of unwillingness or recall bias), leading to an overestimation of the proportion of episodes requiring ambulance call-out. We also cannot exclude the possibility that HCP recall bias influenced participant identification and selection, although a variety of methods were employed to identify eligible individuals. Furthermore, the limited number of consultations for hypoglycaemia follow-up may reflect a lack of detailed recording of discussions about hypoglycaemia during consultations, especially in instances where the cause was known and considered unlikely to recur. The study included patients reporting severe hypoglycaemia at any point within previous 2 years, therefore, patients had a variable period of follow-up before and after the event which may have limited the time available to observe changes in diabetes management. Furthermore, since many patient pathways for linking hypoglycaemia-related ambulance attendances with diabetes services have been implemented since 2014, it is possible that patients requiring ambulance attendance earlier during the study observation period may have been less likely to have been referred to diabetes services than those towards the end of the observation period.

One strength of this study is that participants were recruited from 10 hospitals geographically distributed across England and Wales, so the results may be generalizable to the UK population. In addition, we evaluated emergency and non-emergency hospital resource utilisation, including all diabetes centre consultations, HbA₁c evaluations and HCP-recommended changes to diabetes therapy. This has enabled an evaluation of the temporal
relationship between severe hypoglycaemia and secondary care interventions. However, we were not able to evaluate costs associated with post-hypoglycaemia consultations in primary care; this is worthy of further study.

Conclusions

The results of our study suggest three gaps in the diabetes care pathway warranting further evaluation: (1) lack of a consistent mechanism for reporting by paramedics to primary care and subsequent referral of individuals to specialist diabetes services, (2) lack of a consistent approach to early follow-up of self-reported episodes of severe hypoglycaemia by specialist diabetes services, and (3) low levels of HCP-recommended therapy change and ongoing specialist review following self-reported episodes of severe hypoglycaemia.
References


23 Wang H, Donnan PT, Leese CJ, Duncan E, Fitzpatrick D, Frier BM, et al. Temporal changes in frequency of severe hypoglycemia treated by emergency medical services in types 1


Table 1. Participant demographic and clinical characteristics at data collection

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI, kg/m² (mean [SD]; n=79)</strong></td>
<td>26.8 [4.7]</td>
</tr>
<tr>
<td><strong>Selected comorbidities, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>53 (62%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>41 (48%)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>25 (29%)</td>
</tr>
<tr>
<td>Nerve damage</td>
<td>21 (25%)</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>14 (16%)</td>
</tr>
<tr>
<td>Diabetic foot ulcers</td>
<td>8 (9%)</td>
</tr>
<tr>
<td><strong>HbA₁c, mmol/mol; %, mean (SD)</strong></td>
<td>69 (17); 8.4% (1.6%)</td>
</tr>
<tr>
<td><strong>Insulin therapy, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>MDI</td>
<td>70 (82.4%)</td>
</tr>
<tr>
<td>CSII</td>
<td>5 (5.9%)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (11.8%)</td>
</tr>
<tr>
<td>**Concomitant non-diabetes medication, n (%)</td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td>57 (67%)</td>
</tr>
<tr>
<td>Non-β-blocker antihypertensives</td>
<td>40 (47%)</td>
</tr>
<tr>
<td>β-blockers</td>
<td>13 (15%)</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>8 (9%)</td>
</tr>
</tbody>
</table>

BMI: body mass index; CSII: continuous subcutaneous infusion; MDI: multiple daily injection
Table 2. NHS resource utilisation costs associated with severe hypoglycaemia

<table>
<thead>
<tr>
<th>Resource(s) used</th>
<th>n</th>
<th>Mean cost per episode(^a)</th>
<th>Total cost of episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total resource pathway for ambulance call-outs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambulance call-out (no conveyance)</td>
<td>83</td>
<td>£180.00</td>
<td>£14,940.00</td>
</tr>
<tr>
<td>Ambulance call-out and A&amp;E attendance</td>
<td>11</td>
<td>£359.51</td>
<td>£3,954.56</td>
</tr>
<tr>
<td>Ambulance call-out, A&amp;E attendance and non-elective inpatient admission</td>
<td>5</td>
<td>£2,575.82(^b)</td>
<td>£12,879.10</td>
</tr>
<tr>
<td><strong>A&amp;E attendance without ambulance</strong></td>
<td>10</td>
<td>£126.51</td>
<td>£1,265.06</td>
</tr>
<tr>
<td><strong>Other healthcare resource use</strong></td>
<td>2</td>
<td>£316.75(^c)</td>
<td>£633.49</td>
</tr>
<tr>
<td><strong>No qualified healthcare intervention</strong></td>
<td>29</td>
<td>£0</td>
<td>£0</td>
</tr>
<tr>
<td><strong>All episodes</strong></td>
<td>140</td>
<td>£240.52</td>
<td>£33,672.21</td>
</tr>
<tr>
<td><strong>Total for ambulance call-outs alone</strong></td>
<td>99</td>
<td>£188.57(^d)</td>
<td>£18,668.00</td>
</tr>
</tbody>
</table>

A&E: Accident and Emergency. \(^a\)Mean cost based on number of episodes for each type of resource(s) used, based on NHS reference costs [16]; any differences between mean cost per episode and total cost of episodes are due to rounding. \(^b\)Based on the weighted average daily non-elective inpatient costs; \(^c\)costed as appropriate to type; \(^d\)based on costs for ambulance attendances only (£180) or ambulance attendance with conveyance to hospital (£233), as appropriate.
<table>
<thead>
<tr>
<th>Reason for consultations</th>
<th>Number of consultations (% of n=552)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine diabetes management</td>
<td>280 (51%)</td>
</tr>
<tr>
<td>Foot clinic</td>
<td>103 (19%)</td>
</tr>
<tr>
<td>Hypoglycaemia follow-up</td>
<td>70 (13%)</td>
</tr>
<tr>
<td>Ophthalmology/eye clinics</td>
<td>35 (6%)</td>
</tr>
<tr>
<td>Medication change</td>
<td>12 (2%)</td>
</tr>
<tr>
<td>Nephrology</td>
<td>10 (2%)</td>
</tr>
<tr>
<td>Pump clinic</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Vascular clinic</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Other</td>
<td>35 (6%)</td>
</tr>
</tbody>
</table>
Table 4. Reasons for changes to diabetes treatment during the 2-year observation period

<table>
<thead>
<tr>
<th>Reason for change</th>
<th>Changes during observation period (% of n=119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycaemic event</td>
<td>52 (44%)</td>
</tr>
<tr>
<td>Adverse event</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Personal choice</td>
<td>13 (11%)</td>
</tr>
<tr>
<td>Hyperglycaemia(^a)</td>
<td>8 (7%)</td>
</tr>
<tr>
<td>Clinician/nurse advice</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Not known</td>
<td>31 (26%)</td>
</tr>
</tbody>
</table>

\(^a\)Includes ‘High blood glucose on waking’ reported in 3/8 participants
Figure legends

Figure 1. Participant characteristics at data collection (n=85). Panel (a): age and sex distributions. Panel (b): distribution of duration of diabetes.

Figure 2. Severe hypoglycaemia events and associated emergency resource utilisation during the 2-year observation period. Panel (a): severe hypoglycaemia events/person (total of 140 events in 85 participants). Panel (b): time between episodes of severe hypoglycaemia and hypoglycaemia follow-up consultations (n=60 hypoglycaemia follow-up consultations documented following a severe hypoglycaemic event).

Figure 3. Distribution of HbA1c measured most closely prior to the severe hypoglycaemic events. (HbA1c measured prior to n=119 severe hypoglycaemic events)