

Research: Health Economics

Incidence and care-related costs of severe hypoglycaemia requiring emergency treatment in Andalusia (Spain): the PAUEPAD project*

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Abstract

Aims Hypoglycaemia is a serious medical emergency. The need for emergency medical service care and the costs of hypoglycaemic emergencies are not completely known.

Methods This was a retrospective observational study using Public Company for Health Emergencies (EPES) data for hypoglycaemia in 2012. The EPES provides emergency medical services to the entire population of Andalusia, Spain (8.5 million people). Data on event type, onsite treatments, emergency room visits or hospitalization were collected. Medical costs were estimated using the public rates for healthcare services.

Results From a total of 1 137 738 emergency calls that requested medical assistance, 8683 had a primary diagnosis of hypoglycaemia (10.34 per 10 000 person-years). The incidence of severe hypoglycaemic episodes requiring emergency treatment in the estimated population with diabetes was 810 episodes per 10 000 person-years. A total of 7479 episodes (86%) required an emergency team to visit the patient's residence. The majority of cases (64%) were addressed in the residence, although 1784 (21%) cases were transferred to hospital. A total of 5564 events (65%) involved patients aged > 65 years. Overall mortality was 0.32% (28 cases). The total annual cost of attending a hypoglycaemic episode was €6 093 507, leading to an estimated mean direct cost per episode of €702 ± 565. Episodes that required hospital treatment accounted for 49% of the total costs.

Conclusions Hypoglycaemia is a common medical emergency that is associated with high emergency medical service utilization, resulting in a significant economic impact on the health system.

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Introduction

Diabetes mellitus affects 13.8% of the Spanish population over 18 years of age [1]. Following global trends, the prevalence of the disease in Spain is expected to increase in

future years. Diabetes-associated mortality doubled between 1990 and 2010, and after adjusting the years to reflect disability, the number of healthy years of life that were lost to this disease increased by 70% [2,3]. One of the known causes of death in patients with diabetes is hypoglycaemia [4,5].

Hypoglycaemia is a common adverse complication of treating diabetes. Event rates for severe hypoglycaemia in people with Type 1 diabetes range from 115 to 320 per 100 person-years [6–9]. Severe hypoglycaemia in insulin-treated individuals with Type 2 diabetes has been shown to occur at rates of 10–70 episodes per 100 person-years [6–9]. However, when broader populations of people with Type 2

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What's new?

- This is a retrospective study of all registered hypoglycaemic emergency calls ($n = 8683$) in 2012 that were serviced by the emergency medical services in Andalusia, Spain (8.5 million inhabitants).
- Understanding the incidence of hypoglycaemic emergencies in this population (10.34 per 10 000 person-years) may be valuable for clinical and epidemiological purposes.
- The frequency of calls was lower during the night, but the average urgency was higher than during the remainder of the day.
- Our results indicate the high cost of treating hypoglycaemia as emergency care (€702 per episode).
- The episodes that require referral to a hospital (21%) represented half of the total expenditure.

diabetes are included, the incidence of severe hypoglycaemia ranges from 0 to 3 per 100 person-years in adults with Type 2 diabetes [7]. However, because Type 2 diabetes is more prevalent than Type 1 diabetes, most episodes of hypoglycaemia, including severe hypoglycaemia, occur in people with Type 2 diabetes [8]. Treatment with hypoglycaemic agents, i.e. secretagogues and insulin, and a previous history of hypoglycaemia are powerful risk factors for further hypoglycaemia [6,7,10].

Hypoglycaemia is a frequent cause of hospitalization [11]. Recent evidence has indicated that insulin-related hypoglycaemia is responsible for nearly 100 000 visits to emergency departments in the USA each year [12]. This represents ~10% of the number of emergency department visits from adverse drug reactions per year. The number of visits is particularly high in the elderly. Those over 80 years of age were more than twice as likely as those aged 45–64 years to visit the emergency department and nearly five times as likely to be hospitalized. These data correspond with those of previous studies, which have shown that treatment with insulin and oral hypoglycaemic drugs (sulfonylureas and meglitinides) are among the main adverse drug-event-related causes of hospital admissions in people over 65 years of age [13]. In a follow-up study of self-reported hypoglycaemia in 630 persons with Type 1 and Type 2 diabetes undergoing insulin therapy, Orozco-Beltran *et al.* showed that 30% of respondents who had experienced a severe hypoglycaemia episode (SHE) required an emergency hospital visit following their last SHE and 19% were admitted to hospital [14].

Few studies have reported on the need for emergency medical service care, outcomes, resource utilization and costs of hypoglycaemic emergency care in people with hypoglycaemia. Accordingly, we aimed to determine the incidence and

outcomes of hypoglycaemic episodes that require attention from the Andalusia emergency care system and report the economic impact associated with these interventions.

Patients and methods

The Health Emergency Public Company (EPES, for its initials in Spanish) coordinates outpatient assistance for all emergency care for the Andalusia Autonomous Region, serving the entire population of 8 393 159 in 2012 [15]. This study is embedded in the Emergency Assistance of the Person with Diabetes Project (PAUEPAD, for its initials in Spanish). Institutional review board approval was obtained through the EPES and Investigation Committee, and the requirement for informed consent was waived based on the nature of the study.

We conducted a retrospective observational study of all registered hypoglycaemic calls attended by the EPES between 1 January 2012 and 31 December 2012. Cases that were treated by another emergency medical assistance provider with a final diagnosis of hypoglycaemia must be reported to the EPES, and were also included. Therefore, this study collected all cases of severe hypoglycaemia requiring emergency assistance that occurred in the population during 2012.

As part of their function, the eight EPES coordinator centres systematically gather and register all the information received. The EPES database includes demographic data, the age and gender of the patient, and the date and time of the call. In addition, a computerized system based on the Manchester Triage System was used to determine the urgency of events based on the reported signs and symptoms [16]. The following five urgency categories were included: non-urgent (0), standard (1), urgent (2), very urgent (3) and immediate (4). Medical resources were assigned accordingly.

Episodes were documented as hypoglycaemia if a blood glucose level < 3.9 mmol/l was measured during the episode [10]. After treatment, the emergency team assigned codes to diagnoses using the 9th edition of the *International Classification of Diseases-Clinical Modification* (ICD-9-CM) [17]. Unconsciousness was also recorded.

The annual incidence of hypoglycaemia was calculated using the total population of Andalusia registered in the National Institute of Statistics as of 1 January 2013 [15]. The annual incidence rate (assuming that the majority of cases identified had diabetes) for the Andalusian population with diabetes according to gender and age group was estimated using data on the prevalence of diabetes, as reported in the Di@bet.es Study [18] (Table 1).

The reference time corresponds to the moment that assistance was requested. Events were classified as severe nocturnal hypoglycaemic episodes if the calls were received between 00:00 and 07:59.

Direct costs were estimated using the public prices published by the Andalusia Public Healthcare System [19],

Table 1 Severe hypoglycaemia episodes requiring emergency care (total population and population with diabetes) according to age and percentage of transfers to hospital

| Age (years) | Incidence | | | Patients with diabetes [†] (<i>n</i> = estimated number of patients with diabetes) | | | % Hospital transfers | |
|-------------|--|---------------------------|---------------------------|--|-------------------------------------|-------------------------------------|------------------------|------------------------|
| | Men Total population* (<i>n</i> = number of cases) | Women | All | Men | Women | All | Men | Women |
| 0–17 | 1.07 <i>n</i> = 91 | 1.10 <i>n</i> = 88 | 1.08 <i>n</i> = 179 | 478 (387–584) <i>n</i> = 1895 | 707 (571–864) <i>n</i> = 1,242 | 569 (459–656) <i>n</i> = 3,157 | 41.7 <i>n</i> = 38 | 42 <i>n</i> = 37 |
| 18–30 | 3.69 <i>n</i> = 256 | 3.13 <i>n</i> = 209 | 3.41 <i>n</i> = 465 | 264 (232–297) <i>n</i> = 9,713 | 448 (391–511) <i>n</i> = 4,667 | 323 (295–354) <i>n</i> = 14,380 | 22.6 <i>n</i> = 58 | 20.6 <i>n</i> = 43 |
| 31–45 | 5.33 <i>n</i> = 563 | 3.72 <i>n</i> = 380 | 4.54 <i>n</i> = 943 | 69 (64–75) <i>n</i> = 81,295 | 149 (135–165) <i>n</i> = 25,492 | 88 (83–94) <i>n</i> = 106,787 | 22 <i>n</i> = 124 | 17.1 <i>n</i> = 65 |
| 46–60 | 7.77 <i>n</i> = 649 | 5.15 <i>n</i> = 433 | 6.45 <i>n</i> = 1082 | 32 (29–34) <i>n</i> = 204,567 | 42 (38–46) <i>n</i> = 103,402 | 35 (33–37) <i>n</i> = 307,978 | 23.5 <i>n</i> = 153 | 21 <i>n</i> = 91 |
| 61–75 | 19.53 <i>n</i> = 970 | 19.50 <i>n</i> = 1,079 | 19.52 <i>n</i> = 2,049 | 41 (39–44) <i>n</i> = 234,842 | 68 (64–72) <i>n</i> = 159,301 | 52 (50–54) <i>n</i> = 394,143 | 25.6 <i>n</i> = 248 | 20.6 <i>n</i> = 222 |
| > 75 | 62.60 <i>n</i> = 1,411 | 71.78 <i>n</i> = 2,554 | 68.22 <i>n</i> = 3,965 | 154 (146–162) <i>n</i> = 91,728 | 160 (154–167) <i>n</i> = 159,397 | 158 (153–163) <i>n</i> = 251,125 | 23.4 <i>n</i> = 330 | 18.4 <i>n</i> = 470 |
| Total | 9.48 <i>n</i> = 3,940 | 11.19 <i>n</i> = 4,743 | 10.34 <i>n</i> = 8,683 | 63 (61–65) <i>n</i> = 624,063 | 105 (102–108) <i>n</i> = 453,507 | 80 (78–83) <i>n</i> = 1,077,570 | 24.1 <i>n</i> = 950 | 19.6 <i>n</i> = 930 |

*Incidence rates (events per 10,000 person-years) calculated among the total population, corresponding to confidence intervals of 100%.

[†]Incidence rates among people with diabetes (DM): events per 10,000 person-years (95% CI)

updated for 2012. Transfer distance was calculated from the primary care setting to the corresponding hospital. The estimate excludes the costs of incidents that the physician solved over the phone from the coordinator centre. The costs of hospitalization after emergency assistance and costs resulting from a stay of > 24 h were also excluded from the study.

Data analysis was performed using the PASW statistical package, v. 18.0 (SPSS Inc. Quarry Bay, Hong Kong). The results are presented using the mean and standard deviation for the quantitative variables and the absolute and relative frequencies for the qualitative variables. Confidence intervals (95% CI) were obtained using the exact binomial method. The frequency of SHEs or the mean category of urgency was evaluated using a *t*-test for unequal variance samples. We performed a logistic regression analysis to quantify the influence of sex, age group, time interval, month of referral and hospital location.

Results

During 2012, the EPES coordinator centres answered 1 137 738 calls for assistance in Andalusia [20], of which 8683 (0.76%) were classified as hypoglycaemia requiring assistance. All cases were classified as SHEs because third-party assistance was needed to correct the hypoglycaemic condition [10].

The 8683 SHEs had the following frequency distribution: one SHE, 5990 cases; two SHEs, 841 cases; three SHEs, 212 cases; four SHEs, 63 cases; five SHEs, 8 cases; six SHEs, 9 cases; nine SHEs, 1 cases; and ten SHEs, 2 cases. Thus, 16% of patients requested assistance for more than one episode.

The mean age of the patients was 66 ± 20.2 years (range: 1–107), and 54.6% of patients were women. More than two thirds of the patients were over 60 years of age, and 45.6% were over 76 years of age. The accumulated annual incidence of SHEs requiring emergency care for the study population was 10.34 per 10 000 person-years (11.19 for women and 9.48 for men). In patients over 75 years of age, the annual incidence was 68.22 per 10 000 person-years (Table 1). Data on the estimated accumulated annual incidence of hypoglycaemia in the Andalusia population with diabetes according to gender and age group are shown in Table 1. The incidence rate in the population with diabetes was higher in the two extreme age populations, i.e. 0–30 years: 367 events per 10 000 person-years (95% CI: 329–409); and > 75 years: 158 events per 10 000 person-years (95% CI: 153–163).

Urgency category and the time distribution of the SHEs are shown in Fig. 1. Nocturnal SHEs were less frequent than diurnal SHEs with 0.34 ± 0.03 (*n* = 2297) vs. 0.47 ± 0.09 (*n* = 6386) episodes per hour (*P* < 0.001). Nevertheless, mean urgency category was higher during the night than during the day, with 3.36 ± 0.04 (*n* = 2297) vs. 3.31 ± 0.04 (*n* = 6386) episodes (*P* = 0.01). The mean age of patients treated during the night was similar to that of those treated during the day (66.7 ± 20.1 vs. 66.6 ± 24.6 , *P* = 0.934). There were also no gender differences in treatments between day and night, as follows: 54.7% of the episodes in women occurred at night vs. 54.4% during the day (*P* = 0.804).

The seasonal distribution of SHEs requiring emergency service assistance and the mean urgency category are shown in Fig. 2.

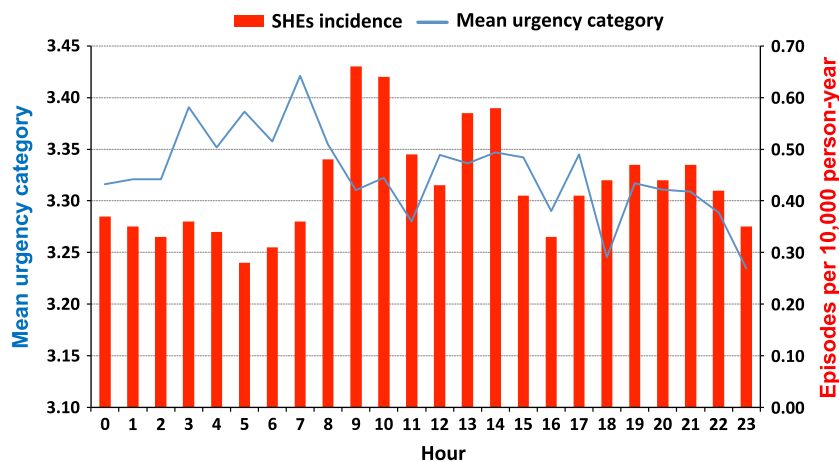


FIGURE 1 Incidence of severe hypoglycaemic episodes (SHEs) ($n = 8683$) and average category of urgency per hour. A computerized system based on the Manchester Triage System [16] was used to determine the urgency of events in the following five categories: non-urgent (0), standard (1), urgent (2), very urgent (3) and immediate (4).

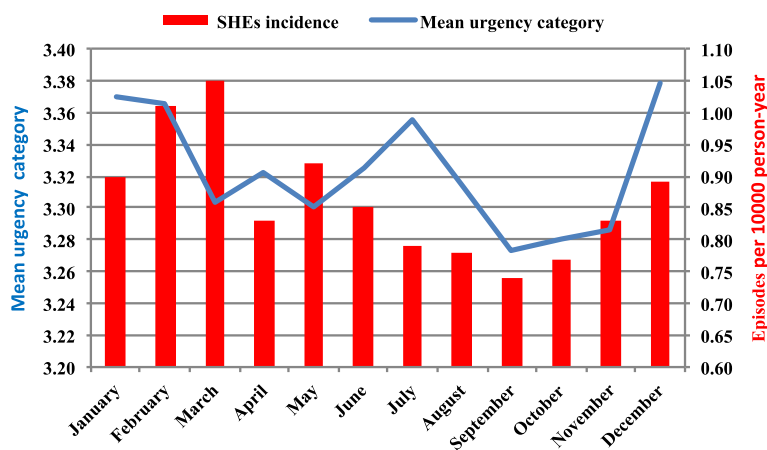


FIGURE 2 Seasonal incidence of severe hypoglycaemic episodes (SHEs) requiring emergency care ($n = 8683$) and average category of urgency. A computerized system based on the Manchester Triage System [16] was used to determine the urgency of events in the following five categories: non-urgent (0), standard (1), urgent (2), very urgent (3) and immediate (4).

In 75% of the cases, hypoglycaemia was recognized by the patient (home blood glucose monitoring) or by family members. In the remaining cases, hypoglycaemia was confirmed during emergency assistance.

Emergency care and resource utilization

Eighty-five per cent of the calls due to hypoglycaemia required a medical emergency team visit to the patient's home, and 13.83% were solved over the phone by the EPES coordinator centres. A small percentage (0.46%) of patients rejected assistance during the telephone calls, and 28 patients (0.32%) died before or while receiving emergency support.

After receiving domiciliary medical assistance, 1784 patients (21%) required a hospital referral. Nearly half (45%) were over 76 years of age, and only 4% were between 0 and 17 years of age. However, hospital referral was more frequent in the 0–17-year-old age group, where 42% of the

episodes required referral to hospital emergency services (Table 1).

Among the hospital referrals, 49% were transported in an ambulance attended by healthcare professionals, and the remaining referrals used a transport ambulance without a medical team. In the 0–17-year-old age group, 77% of the cases required a healthcare professional-aided transfer; for the remaining age groups, half required an ambulance-assisted transfer.

Regarding the factors associated with a hospital referral, we found a higher probability for men [odds ratio (OR) = 1.30, 95% CI: 1.17–1.44, $P < 0.001$] for the time of day between 08:00 and 15:59 (OR = 1.45, 95% CI: 1.27–1.65, $P < 0.001$, reference time interval 0–8 h) and a significantly lower OR for all groups compared with the 0–17-year-old age group (reference). The lowest OR for referral was observed in the 31–45-year-old age group (OR 0.35, 95% CI: 0.25–0.49, $P < 0.001$).

Table 2 Costs per SHE

| | All SHEs | Nocturnal SHEs (00.00 to 07.59) | SHEs requiring emergency hospital care | SHEs causing loss of consciousness |
|--|----------------|------------------------------------|---|---------------------------------------|
| Total direct costs (€ 1000s) | 6093 | 1527 | 2992 | 564 |
| Number of episodes | 8683 | 2287 | 1784 | 558 |
| Direct cost per individual (€) | 702 ± 565 | 668 ± 11 | 1677 ± 304 | 1012 ± 601 |
| Components of the direct cost (€)* | | | | |
| Emergency care in place or residence (%) | 464 ± 273 (66) | 474 ± 252 (71) | 524 ± 311 (31) | 646 ± 264 (64) |
| Transfer | 30 ± 73 (4) | 24 ± 68 (4) | 143 ± 98 (9) | 38 ± 75 (4) |
| Emergency hospital care < 24 h | 208 ± 408 (30) | 170 ± 378 (25) | 1010 ± 0.0 (60) | 328 ± 473 (32) |

*Additional information about the unit costs included in the direct cost components of SHEs is given in the Supporting Information (Table S1).

Costs

The total estimated emergency care costs in 2012 were €6 093 507, and the mean direct cost per episode was €702 ± 565. Episodes requiring referral to hospital emergency rooms (21%) represented 49% of the total expenditure. The components of the direct costs are reported in Table 2. The hospital emergency department cost represented ~30% (€208 ± 408) of the total costs. However, hospitalization costs for children < 17 years of age represented 40% of the total costs.

The costs varied according to patient age from €984 ± 759 for children aged < 17 years to €682 ± 549 for adults aged > 65 years. There were no differences in costs between diurnal and nocturnal hypoglycaemia. SHEs leading to a loss of consciousness were more costly (€1011 ± 601) than those that did not (€680 ± 555).

Discussion

We reported data on emergency medical services' first response care for patients with hypoglycaemia and those patients' clinical outcomes, need for hospitalization, resource utilization and healthcare costs in a large population (8.5 million people). The incidence of hypoglycaemic emergencies in this population (10.34 per 10 000 person-years) obtained from our study may be valuable for epidemiological, clinical and administrative purposes.

The rate of SHEs requesting emergency service assistance for the population with diabetes was 810 per 10 000 person-years. Considering that the incidence of SHEs in adults with diabetes is 300 per 10 000 person-years [7], our data suggest that 30% require assistance from the emergency services. Structured training in self-management could reduce both the rate of SHEs requiring emergency treatment and their associated costs [21].

The time distribution analysis of hypoglycaemia provides novel information from a clinical perspective. The frequency of telephone calls is lower during the night (26.45% of the total) and is higher between 09.00 and 11.00 in the morning. By contrast, the nocturnal calls for assistance were more

urgent, on average, compared with those made during the remainder of the day. These results are consistent with those of Chico *et al.* [22], who observed unrecognized hypoglycaemia in 47–62% of people with diabetes, with 73.7% of all events occurring at night. These data underline the need to improve the prevention and detection of nocturnal hypoglycaemia.

The seasonal distribution of SHEs is also interesting because the frequency is unexpectedly lower during the summer (when people participate in more physical activity). By contrast, the mean urgency is higher during this season.

The increase in direct health costs is the largest contributor to the economic impact of diabetes, especially treatment-related complications, such as those related to severe hypoglycaemia. In the USA, the costs of hospitalization or emergency care for those with diabetes accounted for 21.4% of the total expenditures for diabetes care [23]. According to a recent study conducted in Spain and endorsed by the Spanish Society of Diabetes, the direct health costs of the disease comprised 8.2% of the health expenditures of the National Health System (€5809 million) in 2010. Expenses due to hypoglycaemia could increase the estimated costs to at least €12 million [24]. In 2007, Guisasola *et al.* analysed cases of severe hypoglycaemia from a primary healthcare centre in Spain and estimated that each episode had a price of €384, of which €280 and €104 were related to ambulance costs and emergency care in the primary healthcare centre, respectively. Furthermore, the estimated mean admission cost was €2478 [25]. Our results indicate that emergency care costs are a major component of the total cost of hypoglycaemia care, with an estimated mean direct cost of €702 per episode.

Episodes requiring referral to hospital emergency rooms (21%) represented half of the total expenditure. The results of our study are in agreement with previous studies that demonstrated that most hypoglycaemic events could be treated at home by an emergency response team. Lammert *et al.* reported that between 23 and 25% of people with a severe hypoglycaemic episode in Germany and the UK, respectively, were referred to a hospital emergency care service [26]. In Spain, Orozco-Beltran *et al.* reported that

~ 30% were referred to hospitals [14]. A retrospective analysis of emergency care in a population of nearly 400 000 inhabitants in the UK reported a higher rate of referrals (59%) to the hospital emergency service [27], but in that study, a glucose value < 3.5 mmol/l and parenteral therapy was an inclusion requirement.

A study in a smaller population in the UK recently described similar results on the incidence of SHEs requiring attendance by emergency medical services [28]. However, Farmer *et al.* estimated a mean average cost per emergency call of €363, approximately half of our estimated costs. However, the economic evaluations incorporated different items in each study. The study by Farmer *et al.* did not cover some costs that were included in our study, such as the distance between transfers or the use of a helicopter (four of them were used in our study, leading to an additional cost of €17 280) (Table S1). However, they reported that 35% of people were transferred to the hospital compared with 21% in our results. This finding may be related to the fact that EPES includes doctor supervision in each response and could increase the proportion of SHEs that are solved at the scene.

We recognize several limitations in our study, including the retrospective design. Other limitations include the lack of information regarding data relevant to the risk of hypoglycaemia, such as the treatment of diabetes and the degree of glucose control.

In summary, hypoglycaemia requiring emergency treatment is common and is associated with a significant utilization of healthcare resources and financial impact. More effort is needed to reduce this serious complication, which is mainly related to diabetes treatment. In addition, our study indicates the need for well-structured treatment and hospital transfer protocols that might improve the outcomes and reduce the hospitalization costs for those with hypoglycaemia.

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Competing interests

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Author contributions

RJB researched the data and provided final approval of the manuscript. RJB and FG-P wrote the manuscript, contributed to the data interpretation, and provided critical revisions. GEU contributed to the data interpretation and provided critical revisions. MD-R contributed to the data interpretation and statistical analyses. All the other authors contributed to the discussion and reviewed the manuscript. RJB is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Supporting Information

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

Table S1. Unit costs (2012) of resources, numbers and weights in the total cost of severe hypoglycaemia events requiring emergency care.