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Research: Complications

Hypoglycaemia in adults with insulin-treated diabetes in the UK: self-reported frequency and effects

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Abstract

Aim Few real-life studies of non-severe (self-treated) hypoglycaemic events are available. This survey quantified the self-reported frequency of non-severe hypoglycaemia and its effects in adults with insulin-treated diabetes in the UK.

Methods Adults aged > 15 years with Type 1 diabetes or insulin-treated Type 2 diabetes completed ≤ 4 weekly questionnaires (7–day recall). Respondents with Type 2 diabetes were grouped by insulin regimen: basal-only, basal–bolus and 'other'.

Results Overall, 1038 respondents (466 with Type 1 diabetes, 572 with Type 2 diabetes) completed 3528 questionnaires. Mean numbers of non-severe events per week were 2.4 (Type 1 diabetes; median = 2) and 0.8 (Type 2 diabetes; median = 0); 23% and 26% of non-severe events occurred at night, respectively. Fatigue and reduced alertness were the commonest issues following events (78% and 51% of respondents, respectively). The effects of nocturnal events persisted longer than those of daytime events: Type 1 diabetes = 10.6 vs. 4.9 h ($P = 0.0002$); Type 2 diabetes = 15.3 vs. 5.1 h ($P < 0.0001$). In the week following an event, respondents' blood glucose measurements increased by 4.3 (Type 1 diabetes; 12% increment) and 4.2 (Type 2 diabetes; 21% increment) tests/week. In employed respondents, 20% of events caused work-time loss, more so following nocturnal (vs. daytime) hypoglycaemia: Type 1 diabetes = 2.7 vs. 1.1 h ($P = 0.0184$); Type 2 diabetes = 2.5 vs. 1.6 h ($P = 0.1340$). Most respondents rarely/never informed healthcare professionals about events (Type 1 diabetes = 82%, Type 2 diabetes = 69%).

Conclusions Non-severe hypoglycaemia is common in adults with insulin-treated diabetes in the UK, with consequent health-related/economic effects. Communication about non-severe hypoglycaemia is limited and the burden of hypoglycaemia may be underestimated.

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Introduction

Hypoglycaemia associated with insulin therapy has a negative physical and emotional effect on people with diabetes, causing distress and reducing quality of life [1]. Fear of hypoglycaemia may promote avoidance behaviour and compromise efforts to achieve optimal glycaemic control [2,3], creating a barrier to effective diabetes management, for both people with diabetes and healthcare professionals [4].

Hypoglycaemic events are defined as 'severe' if external assistance is required to effect recovery. Assistance could be from a family member, friend, colleague or healthcare professional [5,6]. Non-severe (or mild) hypoglycaemic events, which account for 88–98% of all events [7–9], are defined by the ability to self-treat [5,6]. Continuous glucose monitoring has demonstrated that 52–84% of individuals with Type 1 diabetes and 57–67% of individuals with insulin-treated Type 2 diabetes develop biochemical hypoglycaemia during sleep, although these events are mostly asymptomatic and their severity is difficult to ascertain [10,11].

Non-severe hypoglycaemia affects daily activities, diminishes quality of life, increases healthcare resource use, and reduces work productivity [7–9,12]. However, real-life studies describing the frequencies and effects of non-severe events are limited in number and quality [1,8,9,12]. Reported frequencies range from 0.1 to 0.8 per week for individuals with Type 1 diabetes and 0.3 to 0.62 per week for individuals with insulin-treated Type 2 diabetes [1,8].

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What's new?

- A fifth of non-severe hypoglycaemia episodes result in loss of work-time. Nocturnal hypoglycaemia has a greater impact on work the next day (through time lost, rescheduling of the working day and difficulty concentrating) than daytime hypoglycaemia, particularly in Type 1 diabetes.
- Non-severe episodes (particularly nocturnal) stimulate a short-term increase in the frequency of blood glucose testing.
- Many adults with diabetes in the UK seldom, or never, inform healthcare professionals about non-severe events, resulting in underestimation of the frequency and potential morbidity of hypoglycaemia.

Recent studies have suggested that 65–92% of individuals with Type 1 diabetes and 55–85% of individuals with insulin-treated Type 2 diabetes do not inform healthcare professionals (general practitioners or specialist diabetes staff) about non-severe events, resulting in under-reporting [3,13]. This may hinder attempts to prevent hypoglycaemia and reduce the effectiveness of education. This was highlighted in the consensus statement by the European Association for the Study of Diabetes and American Diabetes Association [14].

Most studies have focused on the frequency of severe hypoglycaemia, which may not reflect the overall burden of hypoglycaemia [15,16]. Information is also sparse with respect to communication with healthcare professionals about non-severe hypoglycaemia [3] and the health-related and economic effects of non-severe events in the UK. Previous studies reported real-life estimates of the frequency of non-severe hypoglycaemic events in the UK [1,17] and in other European countries [12,16], but results vary because of differing methods of data and sample selection, diabetes type, treatment duration and glycaemic targets.

The principal aim of this study was to determine the self-reported frequency of non-severe hypoglycaemic events in insulin-treated adults with diabetes (Type 1 and Type 2) domiciled in the UK. Secondary objectives were to investigate the duration and effects of non-severe episodes on personal well-being, healthcare resource use, loss of work-time and productivity, in addition to the level of communication about non-severe events between adults and their healthcare professionals.

Methods

This UK study was conducted between September and December 2013, using similar methodology to previous European studies [13,18] with a focus on the economic impact of hypoglycaemia.

Adults with insulin-treated diabetes were identified through an online consumer panel (> 99%) (Medicys Limited, UK), via telephone interviews and referral sampling (from general practitioners and patients; all < 1%). The consumer panel was continuously updated with new members to provide a demographic spread broadly representative of the general diabetes population in the UK (as reflected by national statistics).

Individuals over 15 years of age with Type 1 or Type 2 diabetes who were receiving insulin therapy were included. Participants with Type 2 diabetes were categorized by their insulin regimen: basal-only (i.e. basal insulin, usually taken once daily, often in combination with other anti-diabetes agents), basal–bolus and other forms (e.g. pre-mixed or bolus-only insulin, potentially using a pump).

Respondents completed four online questionnaires, one every 7 days. Questionnaires were adapted from those used in a previous study [19], which were developed using insights from focus groups on the effects of hypoglycaemia [20]. All questionnaires covered the frequency of non-severe events and the effect that the respondent's most recent episode imposed on their use of healthcare resources. Other questions were asked only once; either in the first questionnaire (e.g. questions relating to respondent demographics, discussions with healthcare professionals and the frequency of severe events in the preceding year) or in any of the four questionnaires depending on respondents' previous responses (e.g. questions relating to negative feelings and impact on work productivity following respondents' most recent non-severe episode). Respondents were also asked to report effects on work productivity following an episode during the same or the following day on a scale of 0–10 (0 = no effect, 10 = extremely negative effect).

Weekly frequencies of non-severe events were calculated as averages of all reported weeks across the four questionnaires, with annual frequencies calculated using data from respondents who completed at least the first questionnaire and multiplied by 52. A non-severe event was defined as one causing typical symptoms (e.g. sweating, shaking and/or difficulty concentrating) or an asymptomatic episode with a blood glucose level ≤ 3.1 mmol/l, which did not require assistance. A severe event was defined as one requiring help to effect recovery and/or emergency medical treatment (including hospital attendance/admission). A nocturnal event was defined as one occurring during the night while the respondent was asleep.

Response limits were applied and a logical consistency check removed erroneous responses (e.g. treatment duration exceeding diabetes duration). Respondents were excluded if they did not report their diabetes type or if they misreported any simple demographic characteristics (e.g. a lower age than diabetes duration).

Respondents were anonymized in accordance with European Society for Opinion and Marketing Research and

European Pharmaceutical Market Research Association regulations [21,22]. Simple *t*–tests and Wilcoxon–Mann–Whitney tests were conducted with a 95% threshold for statistical significance.

Results

In total, 1038 adults with diabetes [466 with Type 1 diabetes (45%) and 572 with insulin-treated Type 2 diabetes (55%)] participated, providing 3528 respondent-week records. Full demographics are shown in Table 1.

Table 1 Respondent demographics

	Type 1 diabetes	Type 2 diabetes
Respondents, *n* (%)	466 (45)	572 (55)
Age, mean (SD)	39.8 (13.6)	57.6 (10.6)
Gender, female, *n* (%)	321 (69)	237 (41)
Marital status, *n* (%)		
Single	142 (30)	150 (26)
Married	213 (46)	359 (63)
Partner	111 (24)	63 (11)
Living arrangements, *n* (%)		
Alone	52 (11)	121 (21)
With others	414 (89)	451 (79)
Employed, *n* (%)	292 (63)	198 (35)
Education, *n* (%)		
Primary school	13 (2.8)	16 (2.8)
Secondary school	101 (21.7)	225 (39.3)
Sixth form/college	130 (27.9)	96 (16.8)
University or other further education	196 (42.1)	195 (34.1)
Other	26 (5.6)	40 (7.0)
BMI kg/m^2, mean (SD)	27.2 (6.2)	33.8 (7.5)
Diabetes duration, *n* (%)		
Mean, years (SD)	19.2 (14.0)	12.8 (8.0)
< 2 years	44 (9)	22 (4)
2–5 years	48 (10)	68 (12)
5–9 years	48 (10)	121 (21)
10–14 years	63 (14)	162 (28)
15+ years	263 (56)	199 (35)
Insulin treatment regimen, *n* (%)		
Basal-only insulin	12 (3)	177 (31)
Basal–bolus insulin	345 (74)	301 (53)
Other insulin types	109 (23)	94 (16)
Duration of insulin treatment, *n* (%)		
Mean, years (SD)	18.7 (14.1)	6.0 (5.8)
< 2 years	52 (11)	142 (25)
2–5 years	48 (10)	195 (34)
5–9 years	56 (12)	95 (17)
10+ years	310 (67)	140 (24)
Mean HbA_{1c}*		
Mean mmol/mol (SD);	65 (18.9)	68 (18.7)
NGSP %, (SD)	8.1 (1.7)	8.3 (1.7)
Medical complications,† none reported, *n* (%)	210 (45.1)	139 (24.3)

*Mean HbA_{1c} was based on responses from 239 respondents with Type 1 diabetes and 243 respondents with Type 2 diabetes.
†Response options to the question 'What medical complications do you have as a result of your diabetes?' included: 'none', 'eye problems', 'neuropathy', 'cardiovascular problems/disease', 'renal disease', 'amputations' and 'other'.
NGSP, national glycohaemoglobin standardization programme.

The mean weekly frequency of non-severe events was threefold higher for respondents with Type 1 vs. Type 2 diabetes, and lowest for respondents with Type 2 diabetes receiving basal-only therapy/long-acting insulin alone (Table 2). The median weekly frequency of non-severe events was 2 for respondents with Type 1 diabetes and 0 for all respondents with insulin-treated Type 2 diabetes. On average, respondents experienced ~ 29 (Type 1 diabetes; median = 0) and 11 (Type 2 diabetes; median = 0) nocturnal non-severe events per year. The annual incidence of severe hypoglycaemia was higher for respondents with Type 1 compared with Type 2 diabetes [1.2 (median = 0) vs. 0.4 (median = 0) events] and was similar across the Type 2 diabetes subgroups (0.1–0.5 events).

The most common features of recent non-severe hypoglycaemic episodes were tiredness/fatigue (78% of respondents) and reduced alertness (51%). The average duration of these features was 6.8 h (Type 1 diabetes = 6.1 h; Type 2 diabetes = 7.5 h). The effects of nocturnal non-severe episodes persisted for significantly longer than those that occurred during the daytime: 10.6 vs. 4.9 hours for Type 1 diabetes ($P = 0.0002$) and 15.3 vs. 5.1 h for insulin-treated Type 2 diabetes ($P < 0.001$).

Overall, the proportion of non-severe events leading to contact with a healthcare professional was significantly higher for respondents with Type 2 diabetes than for respondents with Type 1 diabetes ($P < 0.001$; Table 3). For nocturnal non-severe events, the proportion was even higher in respondents with Type 2 diabetes and highest for those receiving basal-only insulin. Following a non-severe event, additional blood glucose tests were made over the subsequent 7 days (4.3 for Type 1 diabetes and 4.2 for Type 2 diabetes), an increase of 12–27% dependent on the insulin regimen employed. This increase in glucose monitoring was greater after a nocturnal event than after a daytime event. In respondents with Type 2 diabetes, the increased testing following nocturnal events was most pronounced in those receiving basal-only insulin.

In employed respondents (61% of Type 1 diabetes and 25% of Type 2 diabetes), 20% of non-severe episodes resulted in loss of work-time (Table 4). Although the mean duration of work-time lost was higher for respondents with Type 2 diabetes than for those with Type 1 diabetes, this was not statistically significant. The work-time lost following nocturnal episodes was longer than that from daytime episodes for respondents with Type 1 diabetes (2.7 vs. 1.1 h, $P = 0.0184$), but was not significant for Type 2 diabetes (2.5 vs. 1.6 h, $P = 0.1340$). Nocturnal events were more likely than daytime events to result in respondents having to reschedule the following work day (Type 1 diabetes: 19% vs. 7%, $P = 0.007$; but was not significant for Type 2 diabetes: 23% vs. 12%, $P = 0.136$) and experiencing significant difficulty concentrating at work (Type 1 diabetes: 53% vs. 36%, $P = 0.024$; Type 2 diabetes: 60% vs. 39%, $P = 0.033$).

Table 2 Self-reported, recalled frequencies of non-severe hypoglycaemic events

All respondents	Type 1 diabetes (n = 466; 1612 rw)	Type 2 diabetes (n = 572; 1916 rw)	Type 2 diabetes subgroups		
			$T2_{BOT}$ (n = 177; 578 rw)	$T2_{BB}$ (n = 301; 1018 rw)	$T2_{Other}$ (n = 94; 320 rw)
NSHEs/week, mean	2.4	0.8	0.6	0.9	0.8
NSHEs/year, mean	126.7	41.5	29.1	48.0	43.4
Daytime NSHEs (%)*	97.5 (77)	30.6 (74)	20.3 (70)	36.1 (75)	31.9 (73)
Nocturnal NSHEs (%)†	29.2 (23)	10.9 (26)	8.7 (30)	12.0 (25)	11.5 (27)
Respondents that experienced ≥ 1 NSHE during the study	**Type 1 (n = 449; 1575 rw)**	**Type 2 (n = 400; 1381 rw)**	**Type 2 diabetes subgroups**		
			$T2_{BOT}$ (n = 96; 326 rw)	$T2_{BB}$ (n = 234; 816 rw)	$T2_{Other}$ (n = 70; 239 rw)
NSHEs/week, mean	2.5	1.1	1.0	1.2	1.1
NSHEs/year, mean	129.7	57.6	51.5	59.9	58.1
Daytime NSHEs (%)†	99.8 (77)	42.5 (74)	36.1 (70)	45.0 (75)	42.6 (73)
Nocturnal NSHEs (%)‡	29.9 (23)	15.1 (26)	15.5 (30)	14.9 (25)	15.4 (27)
Respondents that experienced ≥ 1 nocturnal NSHE during the study	**Type 1 (n = 334; 1190 rw)**	**Type 2 (n = 212; 747 rw)**	**Type 2 diabetes subgroups**		
			$T2_{BOT}$ (n = 48; 166 rw)	$T2_{BB}$ (n = 126; 452 rw)	$T2_{Other}$ (n = 38; 129 rw)
NSHEs/week, mean	2.8	1.4	1.2	1.4	1.5
NSHEs/year, mean	147.6	73.1	64.5	75.2	76.7
Daytime NSHEs (%)‡	108.0 (73)	45.2 (62)	34.1 (53)	48.4 (64)	48.0 (63)
Nocturnal NSHEs (%)	39.6 (27)	28.0 (38)	30.4 (47)	26.9 (36)	28.6 (37)

*Two respondent-weeks were excluded from $T2_{BB}$.
†One respondent-week was excluded from $T2_{BB}$.
NSHE, non-severe hypoglycaemic event; rw, respondent-week; $T2_{BOT}$, respondents with Type 2 diabetes receiving basal-only therapy/long-acting insulin only; $T2_{BB}$, respondents with Type 2 diabetes receiving basal–bolus therapy/short- and long-acting insulin; $T2_{Other}$, respondents with Type 2 diabetes receiving other therapy (e.g. mixed insulin).

Table 3 Direct economic effects of non-severe hypoglycaemic events

Last NSHE across all respondents	Type 1 diabetes	Type 2 diabetes	Type 2 diabetes subgroups		
			$T2_{BOT}$	$T2_{BB}$	$T2_{Other}$
NSHEs resulting in contact with healthcare professionals, n (%)					
Overall*	38 (3)	61 (7)	14 (7)	39 (7)	8 (5)
Diurnal†	29 (3)	40 (6)	7 (5)	27 (7)	6 (5)
Nocturnal‡	9 (3)	21 (10)	7 (16)	12 (9)	2 (7)
Mean increase in BG test strip use within 7 days of a non-severe event, n					
Overall§	4.3	4.2	4.0	4.1	4.6
Diurnal¶	3.9	3.7	3.2	3.8	4.3
Nocturnal**	5.3	5.3	7.2	4.8	5.3
Self-reported weekly frequency of BG tests, mean (SD)††	35.0 (14.5)	19.5 (10.1)	15.1 (8.9)	21.9 (9.9)	20.0 (10.5)

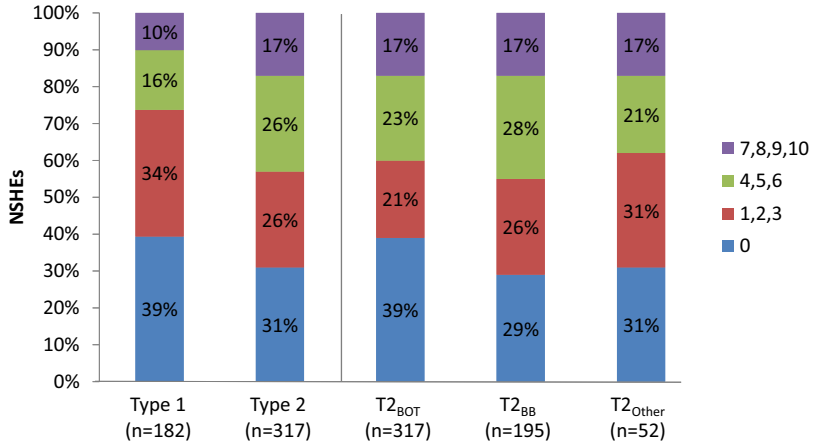
*Base (NSHEs): Type 1 diabetes = 1282, Type 2 diabetes = 884 ($T2_{BOT}$ = 194, $T2_{BB}$ = 536, $T2_{Other}$ = 154). Statistically signifiance difference ($P < 0.001$) for Type 2 vs. Type 1.
†Base (NSHEs): Type 1 diabetes = 998, Type 2 diabetes = 674 ($T2_{BOT}$ = 150, $T2_{BB}$ = 399, $T2_{Other}$ = 125).
‡Base (NSHEs): Type 1 diabetes = 284, Type 2 diabetes = 210 ($T2_{BOT}$ = 44, $T2_{BB}$ = 137, $T2_{Other}$ = 29).
§Base (NSHEs): Type 1 diabetes = 1108, Type 2 diabetes = 851 ($T2_{BOT}$ = 184, $T2_{BB}$ = 516, $T2_{Other}$ = 151).
¶Base (NSHEs): Type 1 diabetes = 845, Type 2 diabetes = 646 ($T2_{BOT}$ = 142, $T2_{BB}$ = 382, $T2_{Other}$ = 122).
**Base (NSHEs): Type 1 diabetes = 263, Type 2 diabetes = 205 ($T2_{BOT}$ = 42, $T2_{BB}$ = 134, $T2_{Other}$ = 29).
††Base (respondents): Type 1 diabetes = 466, Type 2 diabetes = 572 ($T2_{BOT}$ = 177, $T2_{BB}$ = 301, $T2_{Other}$ = 94).
Different bases reflect different populations based on responses provided.
BG, blood glucose; NSHE, non-severe hypoglycaemic event$T2_{BOT}$, respondents with Type 2 diabetes receiving basal-only therapy/long-acting insulin only; $T2_{BB}$, respondents with Type 2 diabetes receiving basal–bolus therapy/short- and long-acting insulin; $T2_{Other}$, respondents with Type 2 diabetes receiving other therapy (e.g. mixed insulin).

Table 4 Indirect economic effect of non-severe hypoglycaemic events in employed respondents

Lost work-time	Type 1 diabetes (n = 812)	Type 2 diabetes (n = 316)	Type 2 diabetes subgroups		
			$T2_{BOT}$ (n = 70)	$T2_{BB}$ (n = 194)	$T2_{Other}$ (n = 52)
NSHEs leading to lost work-time, n (%)	151 (19)	80 (25)	10 (14)	54 (28)	16 (31)
Mean work-time lost after a NSHE (in respondents who lost work-time), min [median (range)]	88.8 [30 (2–1246)]	111.9 [60 (10–643)]	158.0 [120 (30–415)]	119.3 [75 (10–643)]	58.1 [60 (10–120)]

Outcomes of respondents' most recent NSHEs	Type 1 diabetes (n = 284)	Type 2 diabetes (n = 140)	Type 2 diabetes subgroups		
			$T2_{BOT}$ (n = 35)	$T2_{BB}$ (n = 83)	$T2_{Other}$ (n = 22)
Postponement of work appointments, n (%)	10 (4)	11 (8)	4 (11)	7 (8)	0 (0)
Rescheduling of the work day, n (%)	26 (9)	21 (15)	4 (11)	14 (17)	3 (14)
Difficulty concentrating at work, n (%)	111 (39)	62 (44)	10 (29)	43 (52)	9 (41)
Inability to complete a work task in a timely manner, n (%)	208 (73)	86 (61)	27 (77)	45 (54)	14 (64)
Colleagues noticed that the respondent was experiencing hypoglycaemia, n (%)	56 (20)	35 (25)	7 (20)	24 (29)	4 (18)

NSHE, non-severe hypoglycaemic event; $T2_{BOT}$, respondents with Type 2 diabetes receiving basal-only therapy/long-acting insulin only; $T2_{BB}$, respondents with Type 2 diabetes receiving basal–bolus therapy/short- and long-acting insulin; $T2_{Other}$, respondents with Type 2 diabetes receiving other therapy (e.g. mixed insulin).



Type 1, Type 1 diabetes mellitus; Type 2, Type 2 diabetes; $T2_{BOT}$, Type 2 diabetes mellitus respondents receiving basal only therapy/long-acting insulin only; $T2_{BB}$, Type 2 diabetes mellitus respondents receiving basal bolus therapy/short- and long-acting insulin; $T2_{Other}$, Type 2 diabetes mellitus respondents receiving other therapy (e.g. mixed insulin).

FIGURE 1 Effect of employed residents' most severe hypoglycaemic event on work productivity, rated on a 0–10 scale (where 0 indicates no effect and 10 indicates an extremely negative effect during the following day).

On a scale of 0–10, 37% of all respondents gave a mean rating for their last non-severe event of 0 (indicating no effect), 32% gave a rating of 1–3, 19% gave a rating of 4–6, and 12% gave a rating of 7–10 (indicating an extremely negative effect; Fig. 1).

Many respondents (29%) reported that healthcare professionals do not ask them about hypoglycaemic events during routine consultations (Table 5) and 76% reported rarely or never informing healthcare professionals about non-severe events. Mean weekly frequencies of non-severe events were significantly higher for respondents with Type 2 diabetes who rarely or never inform healthcare professionals about non-severe events compared with those who always or usually inform them (0.9 ± 1.2 vs. 0.7 ± 1.1, P = 0.0033). The difference was not statistically different for Type 1 diabetes.

Discussion

This study confirmed that non-severe hypoglycaemia is common in adults with insulin-treated diabetes in the UK, irrespective of diabetes type or insulin regimen. Non-severe episodes (particularly nocturnal events) are burdensome and have effects that persist into the following day. Despite this,

Table 5 Communication about hypoglycaemia between respondents and healthcare professionals

All respondents	Type 1 diabetes (n = 466)	Type 2 diabetes (n = 572)	Type 2 diabetes subgroups		
			$T2_{BOT}$ (n = 177)	$T2_{BB}$ (n = 301)	$T2_{Other}$ (n = 94)
Healthcare professionals do not ask about hypoglycaemic events during appointments, n (%)	112 (24)	187 (33)	62 (35)	90 (30)	35 (37)
Respondents who reported previously experiencing a NSHE (not just in study period)	**Type 1 diabetes (n = 453)**	**Type 2 diabetes (n = 472)**	**Type 2 diabetes subgroups**		
			$T2_{BOT}$ (n = 128)	$T2_{BB}$ (n = 268)	$T2_{Other}$ (n = 76)
Frequency that respondents rarely or never inform healthcare professionals of NSHEs, n (%)	370 (82)	328 (69)	85 (66)	192 (72)	51 (67)
NSHE/week, stratified by the frequency that respondents rarely or never inform healthcare professionals of NSHEs, mean (SD)[†]	2.6 (2.6)	0.9 (1.2)*	0.8 (1.2)*	1.0 (1.3)	0.9 (1.1)

*Indicates statistically significant difference ($P < 0.05$) vs. respondents who always/usually inform healthcare professionals of non-severe events using Wilcoxon–Mann–Whitney test.
[†]One Type 1 diabetes respondent was excluded.
NSHE, non-severe hypoglycaemic event; rw, respondent-week$T2_{BOT}$, respondents with Type 2 diabetes receiving basal-only therapy/long-acting insulin only; $T2_{BB}$, respondents with Type 2 diabetes receiving basal–bolus therapy/short- and long-acting insulin; $T2_{Other}$, respondents with Type 2 diabetes receiving other therapy (e.g. mixed insulin).

communication with healthcare professionals about their frequency and related problems is minimal, suggesting that the frequency and potential burden of hypoglycaemia are probably being underestimated by healthcare professionals and specialist organizations.

The frequencies of non-severe events documented in the present UK study (126.7 per year for Type 1 diabetes; 29.1–48.0 per year for insulin-treated Type 2 diabetes) are similar to those recorded in other European countries using similar methodology [13]; most notably, Sweden (106.1 per year for Type 1 diabetes; 22.4–45.8 per year for insulin-treated Type 2 diabetes) and the Netherlands (105.0 per year for Type 1 diabetes; 24.4–44.7 per year for Type 2 diabetes). However, the annual frequencies are higher than those reported in a prospective study carried out for one month in Tayside by Donnelly *et al.* (41.74 non-severe events per person for Type 1 diabetes and 16.01 non-severe events per person for Type 2 diabetes), although they recorded only symptomatic episodes [8]. This may account for the difference, along with a smaller sample [267 adults, proportionately fewer of whom had Type 1 diabetes (35%)] and diary-based recording of events [8].

The mean weekly frequencies of non-severe events in Type 1 diabetes that were observed in this study in the UK are consistent with findings of studies in Denmark by Pedersen-Bjergaard *et al.* (2.0 events per week) [15] and Kristensen *et al.* (2.2 ± 0.1 events per week) [23]. The mean frequency of non-severe events was lowest for Type 2 diabetes respondents receiving basal-only therapy. This supports the findings of Holman *et al.* who reported that patients on basal insulin experienced fewer grade 1 hypoglycaemic events [defined by a capillary glucose level of 56 mg/dl (3.1 mmol/l) or less in the presence of hypoglycaemic symptoms] than those receiving biphasic or prandial insulin [24].

The negative features of non-severe episodes were similar for all respondents, regardless of diabetes type or insulin regimen, with the three commonest complaints being tiredness/fatigue, reduced alertness and feeling emotionally 'down' or low. This concurs with the observations of two other studies, one of which concluded that hypoglycaemia is a source of anxiety that affects daily living [12] and another which demonstrated that quality of life and health-related utility (assessed via the Short Form 36 and European Quality of Life – 5 Dimensions measures, respectively) decreased with increasing frequency and severity of hypoglycaemia [7].

Non-severe hypoglycaemic episodes increased contact with healthcare professionals and frequency of blood glucose measurements. Although more frequent blood glucose measurement may help to prevent non-severe events in the short term [2], the increased use of test strips represents a direct healthcare cost. Initiatives to increase recognition of non-severe events in people with diabetes may help lower the risk of non-severe events, with consequent economic benefit.

Indirect economic effects of non-severe episodes (particularly nocturnal events) included lost work-time and reduced work productivity. Overall, 20% of non-severe episodes resulted in lost work-time, consistent with a previous report [19]. However, the resulting length of work-time lost (1.6 h) was considerably shorter than that reported by Brod *et al.* (9.9 h) [19], although it was not revealed in that internet-based study whether respondents were aware before enrolment that the survey related to hypoglycaemia. Thus, it is possible that this difference may be attributed to selection

bias towards those who had experienced hypoglycaemia. In addition, the respondent base was derived from several countries and may have differed considerably [19].

Nocturnal episodes had a greater impact on subsequent respondent well-being and work-time on the following day compared with daytime episodes. This is consistent with observations from a previous European study [18] and indicates that nocturnal episodes have significant consequences. However, it is difficult to determine the severity of hypoglycaemic events that occur during sleep, and continuous glucose monitoring has shown that hypoglycaemia during sleep is frequently of longer duration than during waking hours [25–27].

In view of the statistically significant association between infrequent reporting of non-severe events to healthcare professionals and higher event frequencies for Type 2 diabetes respondents, the present results support the premise that frequency of non-severe events is underestimated in clinical practice. Fear of being perceived to have unsatisfactory glycaemic control may contribute. This is supported by the fact that annual rates of severe hypoglycaemia self-reported by Danish adults with Type 1 diabetes declined by more than 50% in the year following the implementation of stricter European Union regulations for Group 1 driving licences [28]. However, this communication gap may represent a failure of healthcare professionals to address the potential problem of hypoglycaemia. This may be particularly true for those with Type 2 diabetes who may not be as experienced or as well informed about insulin usage and therefore less likely to understand the interactions of insulin, food intake and exercise and less able to manipulate their insulin doses appropriately on their own.

Study limitations have been reported previously [13,18]. Despite claims to be representative of the general diabetes population, recruitment through online consumer panels may still have resulted in bias. For example, the majority (69%) of respondents with Type 1 diabetes in this study were female.

Furthermore, data were not weighted according to any demographic variables and study participation required an adequate degree of computer literacy. This may have introduced selection bias, although the rate of computer and internet usage in the UK is high (83.6%) [29]. To minimize participation bias, respondents were not informed that the survey related to hypoglycaemia before enrolment. The high proportion of basal–bolus users may also reflect potential selection bias, suggesting those with more intensive regimens may be more likely to respond to a questionnaire.

Diminishing response rates (90%, 82% and 68% of respondents completed questionnaires two, three and four, respectively) may indicate that later questionnaires were completed by respondents who experience non-severe events more or less regularly than average. This may have resulted in misreporting. However, an analysis of data from the similar European study (utilizing very similar methodology) did not support any trends towards a higher/lower frequency of non-severe events in later questionnaires [13].

Respondents were required to recall the frequency of non-severe hypoglycaemic events experienced in the last 7 days. An earlier study in Type 1 diabetes demonstrated good concordance between retrospective recall of non-severe events during the preceding week and prospective recording of events over the same time period, suggesting that it was appropriate [9].

This study has confirmed that non-severe events are common in adults with Type 1 and insulin-treated Type 2 diabetes in the UK, and have significant, long-lasting effects for personal well-being, healthcare resource use and work productivity. Nocturnal episodes cause greater problems and potential morbidity, particularly in Type 1 diabetes. Despite this, communication about non-severe hypoglycaemia between healthcare professionals and people with diabetes is minimal, suggesting that the frequency and morbidity of hypoglycaemia are being underestimated. This indicates an unmet need for more education on self-management of hypoglycaemia in the UK.

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Competing interests

MM Jensen is an employee and shareholder of Novo Nordisk. BD Chubb is an employee of Novo Nordisk. Professor Frier has received honoraria from Novo Nordisk for membership of advisory boards and speakers' bureau.

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