

# Frequency, Severity, and Morbidity of Hypoglycemia Occurring in the Workplace in People With Insulin-Treated Diabetes

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**OBJECTIVE** — Hypoglycemia was examined in regularly employed people with insulin-treated diabetes to ascertain the frequency and consequences of this problem in the workplace.

**RESEARCH DESIGN AND METHODS** — A prospective 12-month survey of 243 employed people (age range 20–69 years) with insulin-treated diabetes was performed to record the frequency, severity, and morbidity of hypoglycemia occurring at work. Details of hypoglycemic episodes included time of day, place, activity, causation, blood glucose, treatment, and morbidity. Serial HbA<sub>1c</sub> measurements were recorded.

**RESULTS** — A total of 1,955 mild (self-treated) episodes of hypoglycemia (8 per person per annum) and 238 severe (requiring external help) episodes (0.98 per person per annum) were recorded. Of the severe hypoglycemic episodes, 148 (62%) occurred at home, 35 (15%) occurred at work in 27 (11%) people (0.14 episodes per person per annum), and 54 (23%) occurred elsewhere; 52% of severe episodes occurred during sleep. Of the severe hypoglycemic episodes reported, adverse events were described in 54 (23%), with 29 losing consciousness (14%), 21 having a seizure (9%), 4 (2%) sustaining a head injury, 5 (2%) suffering another injury, 3 (1%) injuring someone else, and 2 (1%) damaging property. Severe hypoglycemia in the workplace was associated with six episodes of minor soft-tissue injuries.

**CONCLUSIONS** — In this cohort, severe hypoglycemia in the workplace was uncommon and seldom caused disruption or serious morbidity. On the basis of the frequency and severity of hypoglycemia observed in the present study, restriction of employment opportunities for most people with insulin-treated diabetes may be difficult to justify.

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**H**ypoglycemia is a common side effect of insulin therapy (1) and is perceived to present a significant risk for certain occupations. Restrictions can be placed on prospective or current employees with diabetes, which limit their employment opportunities in Eu-

rope and North America (2–4). This may comply with health and safety legislation (5,6) but may not be compatible with employment legislation (7,8). Despite disability discrimination legislation, which now exists in many developed countries, employment opportunities in certain in-

dustries are restricted for people who have insulin-treated diabetes (2,3). In the U.K., recommendations for assessing medical fitness to drive (9) are sometimes used inappropriately by occupational physicians to restrict employment for people with insulin-treated diabetes, who are at risk of developing hypoglycemia in the workplace.

This present prospective study sought to quantify the frequency with which mild and severe hypoglycemia occurs in the workplace in a group of people with insulin-treated diabetes who were in regular employment. The 12-month study aimed to evaluate the consequences of any adverse events associated with episodes of hypoglycemia, with particular reference to daily work.

## RESEARCH DESIGN AND METHODS

The study was conducted in a large diabetes center (6,000 patients) in Edinburgh (population 0.5 million), which is the capital of Scotland, offering employment in major government, educational, legal, and financial sectors but with no significant manufacturing industry. This is reflected in local employment opportunities. The Medical Research Ethics Committee of Lothian Health approved the study, which was funded by the principal British charity for diabetes (Diabetes UK). The study was conducted independently by the Institute of Occupational Medicine in Edinburgh, which has extensive experience of research in the field of occupational medicine.

There is no reliable up-to-date system in the U.K. for relating medical records to employment. Thus, potential participants who were receiving insulin therapy were approached directly to ascertain if they were in employment and were eligible for inclusion in the study. There were no exclusion criteria other than being unemployed or not receiving insulin therapy. People with insulin-treated diabetes in employment who were attending the dia-

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**Abbreviations:** DCCT, Diabetes Control and Complications Trial.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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**Table 1—Distribution of jobs held in the past 12 months by major standard occupational classification and standard industrial classification category**

Job category	Number of jobs	Percent	Industry category	Number of jobs	Percent
Managers and administrators	60	19	Agriculture, hunting, and forestry	1	0
Professional	54	18	Fishing	2	1
Associate professional and technical	60	19	Mining and quarrying	2	1
Clerical and secretarial	45	15	Manufacturing	22	7
Craft and related	16	5	Electricity, gas, and water supply	5	2
Personal and protective service	33	11	Construction	10	3
Sales	11	4	Wholesale and retail trade	21	7
Plant and machine operatives	7	2	Hotels and restaurants	6	2
Other	15	5	Transport, storage, and communication	22	7
Missing	6	2	Financial intermediation	41	13
			Real estate, renting, and business activities	42	14
			Public administration and defense	21	7
			Education	26	8
			Health and social work	70	23
			Other community, social, and personal service	10	3
			Private households with employed persons	1	0
			Missing	5	2
Total	307	100	Total	307	100

Columns total to more than 243 because some individuals held more than one job in the previous year. Each cell contains number of jobs and percentage of column total.

betes outpatient clinic at the Department of Diabetes in the Royal Infirmary of Edinburgh during the period from September 1998 to the end of December 1999 were offered the opportunity to participate in the study. Eligible patients who agreed to take part in the study completed a recruitment questionnaire before formal enrollment into the study. Written informed consent was obtained after the nature of the study had been explained.

A total of 243 people with insulin-treated diabetes (age range 20–69 years), of whom 216 had type 1 diabetes, were recruited. Twice-daily insulin therapy in the form of soluble and NPH was used by 51 patients, and the remainder were using multiple insulin injections of preprandial soluble or fast-acting insulin analogs with bedtime NPH.

Demographic data, contact details, years of education, and height and weight were recorded. The information collected in the recruitment questionnaire included personal details, including occupation and history of diabetes. Their occupation, by both job and industry category, is shown in Table 1. Diabetes history included year of diagnosis, history of treatment with insulin, current insulin regimen and dose schedule, presence of

diabetes complications, frequency of self-monitoring of blood glucose, and a self-assessment of their symptomatic awareness of the onset of hypoglycemia using a validated scoring system. Seven (3%) patients had impaired awareness. Mild hypoglycemia was defined as any symptomatic episode that was self-treated. Severe hypoglycemia was defined as an episode that required treatment by another person and was associated either with a blood glucose concentration of <2.8 mmol/l or with prompt recovery after administration of oral carbohydrate, or the parenteral administration of dextrose or glucagon (10). The participant's history of severe hypoglycemia was documented to ascertain date of first episode, total number of episodes, number of episodes in the preceding year, where they had occurred, and any associated morbidity. The results of HbA<sub>1c</sub> values were obtained from the participant's medical notes at recruitment, at 6 months, and at 12 months. Glycated hemoglobin (HbA<sub>1c</sub>) was assayed using high-performance liquid chromatography adjusted to the Diabetes Control and Complications Trial (DCCT); the local nondiabetic range was 5.0–6.5%.

An occupational history was obtained

for all jobs performed in the 12 months preceding the study. This included job and industry type, hours worked, shift patterns used, and self-reported exposure to hazardous situations, e.g., moving machinery, working at heights, working alone, and driving. These occupations were classified using the standard occupational classification (11), and the industry type was classified using the standard industrial classification (12). The allocation to major occupational and industrial classification categories showed that over half of the participants were employed in jobs from the managerial, professional, and associate professional categories and were based in the health, financial, and business industries. Around a third of the study group had jobs that required them to work in isolation, and a third had jobs that involved driving. A total of 34 (14%) participants reported that their job involved working at heights.

During the prospective study, each participant was requested to complete a monthly report. This detected any changes in contact details, employment history, or insulin treatment. The participants completed a form for every episode of hypoglycemia that they experienced.

**Table 2—Distribution of sex and severe hypoglycemic episodes during the 12-month follow-up period by age-group**

	Severe hypoglycemic episodes during the 12-month follow-up period					All
	Male	None	1	2	>2	
Age-group (years)						
20–29	18 (14)	29 (81)	3 (8)	0 (0)	4 (11)	36
30–39	30 (23)	43 (58)	19 (26)	6 (8)	6 (8)	74
40–49	49 (38)	50 (68)	12 (16)	5 (7)	7 (9)	74
≥50	31 (24)	38 (64)	4 (7)	5 (9)	12 (20)	59
All	128 (53)	160 (66)	38 (16)	16 (7)	29 (12)	243

Data are n or n (%).

This provided information on date and time of each event, location, activity at onset, associated symptoms, details of treatment, occurrence of any adverse events, requirement for subsequent time off work, and the possible cause of the episode. Where an episode was severe and required external assistance, the person who treated the participant was asked to provide additional information. This included date and time of the episode, how he or she was related to the participant, what if anything he or she had observed about the participant in relation to the event, any adverse consequences, identified causation of the episode, the nature of the treatment administered, and any other comments. Blood glucose was recorded if it had been measured at the time of the hypoglycemia.

### Statistical analysis

Mild and severe hypoglycemic episodes were analyzed separately and compared further against the data collected at recruitment. Statistical analysis was performed to provide SDs and *P* values for the differences between individuals who had reported mild hypoglycemia and individuals who had not. The analysis was performed using Minitab (Minitab Inc.).

The episodes of severe hypoglycemia were analyzed using the same methods as for mild hypoglycemia. Logistic regression methods were used to examine the association between the risk of experiencing an episode of severe hypoglycemia during follow-up and the data collected at recruitment. Univariate and multivariate logistic regression analysis was performed using the GENSTAT 5 statistical package (13).

**RESULTS**— The retention of participants throughout the study was excep-

tionally high at 98%. Only seven participants did not complete the study, two of whom had to withdraw because they moved away. The other five who stated that they no longer wished to take part were not questioned further. The percentage of data returned each month was also high, being in excess of 90% for the duration of the study.

### Mild hypoglycemia

A total of 1,955 episodes of mild hypoglycemia were reported, with an incidence of 8 per person per annum. Of these episodes, 1,077 (55%) occurred at home, 580 (30%) occurred at work, and 289 (15%) occurred elsewhere. Of the 580 episodes of mild hypoglycemia that occurred at work, additional data were provided on 563 as to whether any time off from work was required as a consequence of the hypoglycemia. Nineteen participants reported that they had required time off from work (5–30 min; mode 5 min; median 10 min; mean 12.8 min). The one adverse event reported at work incurred damage to property.

### Severe hypoglycemia

A total of 238 episodes of severe hypoglycemia were reported by 83 (34% of study population) of the 243 participants (overall incidence 0.98 episodes per person per annum). Fifty-four (22%) reported one to two episodes of severe hypoglycemia, 16 (7%) reported three to five episodes, and 13 (5%) reported more than five episodes of severe hypoglycemia. Twenty-seven (11%) of the participants reported 35 severe hypoglycemia episodes at work (overall incidence of 0.14 episodes per person per year). The age-group distribution is shown in Table 2. Participants aged between 30 and 39 years were most likely to have reported severe hypoglycemia

than individuals ≥40 years, whereas the lowest frequency of severe hypoglycemia occurred in participants aged <30 years.

### Time of hypoglycemia

Of the severe hypoglycemia episodes reported, 124 (52%) occurred while the participant was asleep.

### Hypoglycemia and sex

In the present study, a sex difference was observed, with women reporting more episodes of severe hypoglycemia in the workplace and elsewhere; 17 women (15%) experienced severe hypoglycemia at work compared with 10 (8%) men, and 30 women (26%) experienced severe hypoglycemia elsewhere compared with 26 men (20%). This contrasted with the retrospective data obtained in the present study, where the reported prevalence of severe hypoglycemia was similar between the sexes (men:women, 27%:34%). During the 12-month study, 47 (41%) women experienced episodic severe hypoglycemia during follow-up compared with 36 (28%) men. The risk of experiencing severe hypoglycemia in men was significantly lower than that in the women by 0.57 (95% CI 0.33–0.97), which was significant statistically.

### Severe hypoglycemia in the workplace

Of the 83 patients who reported a severe hypoglycemic episode during the prospective study, 27 (11%) experienced one or more of these episodes of severe hypoglycemia at work, with detailed information being provided for 35 episodes. A total of 22 people experienced one episode, 2 recorded two episodes, and 3 recorded three episodes occurring at work. The overall incidence of severe hypoglycemia at work was 0.14 episodes per patient per year. No significant risk factors were identified to predict when the risk of experiencing severe hypoglycemia at work was greater than the risk of severe hypoglycemia occurring elsewhere. Individuals who reported severe hypoglycemia occurring anywhere were less likely to be working alone, with machinery, or with toxic substances than those participants who did not report severe hypoglycemia. Furthermore, those participants who reported severe hypoglycemia at work were less likely to have a job that involved driving than those participants who reported severe hypoglycemia oc-

Table 3—Distribution of diabetes variables and demographic variables by severe hypoglycemic episodes during the 12-month follow-up period

	Severe hypoglycemic episodes during the 12-month follow-up period				P
	None	1	2	>2	
Mean insulin units	52.0 ± 19.4	53.4 ± 17.3	53.5 ± 12.5	51.8 ± 19.1	0.97
BMI (kg/m <sup>2</sup> )	26.6 ± 4.3	26.6 ± 4.6	26.3 ± 2.4	26.8 ± 5.1	0.99
Average HbA <sub>1c</sub> (0, 6, 12 months)	9.1 ± 1.3	9.0 ± 1.0	9.2 ± 1.5	8.4 ± 0.9	0.03

Data are means ±SD. P values are given for differences between the three groups; a value of <0.05 indicates statistically significant differences at the 5% level.

curing elsewhere or those who had not experienced severe hypoglycemia.

### Severe hypoglycemia, glycemic control, and history of diabetes

At recruitment, the mean HbA<sub>1c</sub> was 9.1% for the group. The average HbA<sub>1c</sub> concentration over the 12-month follow-up period was significantly lower (HbA<sub>1c</sub> 8.4% ± 0.5, 95% CI 7.94–8.84) in participants who experienced more than two episodes of severe hypoglycemia ( $P = 0.03$ ) when compared with individuals who had reported two or less episodes of severe hypoglycemia. The duration of diabetes was significantly greater for participants who experienced severe hypoglycemia during the 12 months of the study when compared with individuals who did not report severe hypoglycemia ( $P < 0.03$ ). No differences were observed between people who reported severe hypoglycemia and those who did not, with respect to current age, age at diagnosis, presence of impaired awareness of hypoglycemia, total daily insulin dose, or BMI.

An association was found between the mean HbA<sub>1c</sub> (average of three measurements during the year) and a record of more than two episodes of severe hypoglycemia during the year of study, which was of borderline statistical significance at the 5% level ( $P = 0.07$ ). For a 1% increment in mean HbA<sub>1c</sub> over the year, the risk of experiencing severe hypoglycemia was lower by 0.81 (95% CI 0.64–1.01). Compared with individuals who reported no severe hypoglycemia in the 12 months preceding the study, those participants who reported two or more episodes of severe hypoglycemia were eight times more likely to suffer severe hypoglycemia during the 12-month follow-up period. No associations were observed with age, daily insulin dose, BMI, number of injections of insulin given per day, or frequency of self-monitoring of blood glucose. The distribution of demo-

graphic variables and diabetes variables are shown in Table 3.

**CONCLUSIONS**— Although hypoglycemia is a common side effect of insulin therapy, it is not known how often it occurs in the workplace. Recall of episodes of mild hypoglycemia is relatively accurate for up to a week after it occurs and up to a year for severe hypoglycemia (10,14). The overall frequency of mild hypoglycemia documented in the present study is lower than in unselected populations with type 1 diabetes (10,15), but overall glycemic control was suboptimal. Various factors may cause underreporting of hypoglycemic episodes, including impaired awareness of hypoglycemia, which increases with duration of diabetes (10); unidentified nocturnal hypoglycemia (16); asymptomatic biochemical hypoglycemia (17); and the effect of neuroglycopenia causing short-term memory impairment (18). Complete amnesia of the event may be associated with severe hypoglycemia. Infrequent blood glucose monitoring and absence of a written record may also contribute. The reliance on subjective symptoms of hypoglycemia, without verification by simultaneous estimation of blood glucose, affects the incidence of self-reported hypoglycemia (19). The definitions of mild and severe hypoglycemia that were used in the present study have been used in many previous studies (20–22) including the DCCT (17,23).

A sufficient number of episodes of severe hypoglycemia were recorded in 1 year to allow a meaningful analysis. The high proportion of nocturnal episodes of severe hypoglycemia in the present study is similar to the findings in the DCCT (17,23), but in that larger study, the sex difference observed differed from the present study in that severe hypoglycemia was more common in males (23). However, the DCCT included adolescent patients, which may have influenced the sex

difference. Although the mean HbA<sub>1c</sub> of 9.1% in the present cohort indicates suboptimal control, it is similar to the level maintained in the conventionally treated group in the DCCT (23). However, it is possible that to limit the risk of severe hypoglycemia at work, employees deliberately eschew strict glycemic control.

During the 12 months of the study, one-third (34%) of the study population experienced one or more episodes of severe hypoglycemia. This annual prevalence is very similar to that reported in previous surveys of populations of people with insulin-treated diabetes (10,15,17, 20,21,24). In the present study, 83 patients experienced a total of 238 episodes of severe hypoglycemia. The self-reported incidence of severe hypoglycemia was 0.5 episodes per patient per year in the year preceding recruitment, which is lower than the incidence rates of 1.1–1.7 episodes per patient per year reported previously in Northern European studies (10,20–22). However, these previous surveys were carried out in unselected populations of people with type 1 diabetes and included people with impaired awareness of hypoglycemia and other risk factors that promote a higher frequency of severe hypoglycemia (22). Impaired awareness of hypoglycemia could pose a significant risk to normal working efficiency. The present study did not deliberately exclude participants who had impaired awareness of hypoglycemia, but in this cohort, few people in employment appeared to suffer from this problem, with only 3% having evidence of this syndrome compared with a prevalence of impaired awareness of hypoglycemia of ~25% in unselected populations of type 1 diabetes (25). It is possible that some degree of self-selection has occurred, with some people with impaired hypoglycemia awareness having ceased working, which may also partly explain the observed sex differences in that severe hypoglycemia was more common in women (23). Sex-

specific differences have been noted in the counterregulatory hormonal responses to hypoglycemia in type 1 diabetes, with women having a weaker response than men (26). This may increase their risk of severe hypoglycemia, as was observed in the present study. The lower prevalence of impaired awareness may explain the lower overall frequency of severe hypoglycemia recorded in the present cohort compared with previous surveys in our center (20), in Denmark (10), in the Netherlands (21), and in a multicenter study conducted in Denmark and England (15), all of which examined unselected populations with insulin-treated diabetes. In the present study, the incidence of 0.98 episodes per patient per year recorded prospectively suggests that retrospective recall may underestimate the frequency of severe hypoglycemia.

The practical aspects of recruiting people with insulin-treated diabetes who were in employment were considered to be more feasible in the setting of a specialist outpatient clinic. The relatively limited range of occupations of the participants recruited to the present study suggests a degree of selective participation. A possible explanation is that those who work in managerial, administrative, and professional occupations may be more willing to participate in prospective surveys than people who work in manual or nonskilled occupations. A random sample of 108 attendees at the diabetes clinic was subsequently asked to provide information on their occupations, and these data were compared with the study group. The random sample contained fewer people in managerial, administrative, professional, and clerical jobs and more in sales, personal and protective services, and craft. This observation supports the contention that participation in the study involved a degree of self-selection, so that the study population was less representative of the diabetic population in employment. In addition, regularity of clinic attendance may vary between different occupational groups, and the population attending a diabetes specialist clinic may not be representative of the entire diabetic population in a community setting. Caution must be exercised when extrapolating the results of the present study to the entire population of people with insulin-treated diabetes, because lower social class is associated with a higher risk of severe hypoglycemia (27).

On the basis of the self-reported working practices documented at recruitment in the present study, working in isolation was the most common work practice that could be considered to be hazardous with respect to the development of hypoglycemia. The frequency of severe hypoglycemia was similar in this and other subgroups, either at work or elsewhere, except where the job involved driving. Among individuals whose job necessitated driving, the incidence of severe hypoglycemia at work was lower than elsewhere. This may indicate either a degree of preselection of people who are at greater risk of hypoglycemia by the individual or by employers or may be the effect of restriction of driving licenses by the licensing authorities. Participants reported no motor vehicle crashes associated with severe hypoglycemia during this present study. One "near miss" while driving during mild hypoglycemia was reported.

Whereas hypoglycemia was common in this cohort of people with insulin-treated diabetes who were in employment, with an annual prevalence of hypoglycemia occurring at work being 51%, only 11% experienced severe hypoglycemia. Only six severe hypoglycemic events at work resulted in an adverse outcome, and none were serious. After an episode of mild hypoglycemia, very little time was lost at work, with the maximum being 30 min, while after an episode of severe hypoglycemia, one person was absent for 1.5 days. Although the risk factors for severe hypoglycemia are well known (1), any person receiving insulin therapy is potentially at risk of hypoglycemia, and the results of the present study should not promote complacency among people with insulin-treated diabetes in employment.

Whereas the inherent risk of severe hypoglycemia can never be eliminated in people treated with insulin, as a result of this survey, an evaluation of risk can be made on an individual basis. This would be used in the assessment of fitness to work where there is substantial knowledge of the workplace. The risk of severe hypoglycemia is higher for individuals with a positive history for severe hypoglycemia, including the total number of previous episodes, particularly in the preceding year; in those who have an average HbA<sub>1c</sub> of 8.4% or lower; in those who have a longer duration of diabetes (as with each 5-year increment in duration of diabetes, the risk of severe hypoglycemia

increased by 1.16 [95% CI 1.13–1.18]); and in those who do not regularly attend a specialist clinic for diabetes. A careful evaluation of the hazards in the workplace, with an assessment of the risks should an episode of severe hypoglycemia be experienced, in conjunction with the evaluation of risk of severe hypoglycemia, may allow people with insulin-treated diabetes to be employed in areas that have previously been restricted.

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