ORIGINAL ARTICLE

Diabetes management and daily functioning burden of non-severe hypoglycemia in Japanese people treated with insulin

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ABSTRACT

Aims/Introduction: The present study investigated the impact of non-severe hypoglycemic events (NSHE) on patients' diabetes management, daily functioning and well-being.

Materials and Methods: A survey assessing the impact of NSHEs was completed by insulin-treated Japanese people with diabetes, aged ≥20 years with self-reported diabetes, who had experienced at least one NSHE in the past 3 months. Survey questions captured reasons for and the length of the event, and impacts on diabetes management, daily functioning, sleep and well-being.

Results: A total of 3,145 people with type 1 diabetes mellitus and type 2 diabetes mellitus were screened, of which 411 respondents were eligible. Increased glucose monitoring was reported by 57 and 54% of respondents after daytime and night-time NSHE, respectively. The average number of additional glucose monitoring tests was 2.4 and 3.0 for daytime and night-time NSHE. Among all respondents, 19% (daytime) and 16% (night-time) changed their insulin dose after an NSHE. After a daytime NSHE, 25% of respondents reported a negative impact on their daily activities or work. After a night-time NSHE, 34 and 23% of respondents reported a negative impact on sleep and next day emotional state, respectively.

Conclusions: NSHEs have a negative impact on the diabetes management, daily functioning, sleep and well-being of Japanese patients.

INTRODUCTION

Non-severe hypoglycemic episodes (NSHEs), defined as self-treated hypoglycemia, are a common side-effect of insulin therapy, affecting patients with type 1 and type 2 diabetes[1]. Estimates for the incidence of NSHE range between 31.2 and 83.2 episodes per year in type 1 diabetes, and 4.16 and 15.6 episodes per year for insulin-treated type 2 diabetes[2–4].

Beyond the acute phase of hypoglycemia, NSHEs have prolonged negative effects on patients' psychosocial health (fear of hypoglycemia), diabetes management (skipping/reducing insulin doses), and wider economic consequences for both the individual and society through absenteeism, reduced productivity and excess treatment costs[5–7]. Despite a growing body of evidence highlighting the negative clinical and psychosocial impact of NSHEs and their economic importance, they remain underrecognized by the wider medical community and underreported by patients themselves[6,8,9].

Through an improved understanding of the effects of NSHEs, it might be possible to optimize diabetes management, and thereby reduce the frequency of hypoglycemia and its burden on patients. The aim of this survey was to assess the impact of daytime and night-time NSHEs on patients' daily lives, functioning and well-being, adherence to medications, productivity, and resource utilization in a quantitative manner in a Japanese population.

METHODS
Survey development and administration
To assess the impact of NSHE, a survey was developed based on the literature, expert input and interviews with 78 persons with either type 1 diabetes or type 2 diabetes who had recently

experienced an NSHE, in nine focus groups across four countries (USA, UK, Germany and France)[10]. Survey items were developed based on a qualitative analysis of the expert input and the persons' with diabetes interviews, and cognitively debriefed and pilot tested in English in nine persons who met the same eligibility criteria as the focus groups. These steps were carried out to ensure content validity (relevant questions), and to ensure that the questions had face-validity with the respondents (e.g., no unfamiliar/strange words or concepts). The final survey was translated into Japanese using a forward and backward translation process in conjunction with separate patient and physician focus groups. The survey was administered through a secure Internet server in Japan. The survey took approximately 20 min for respondents to complete.

NSHEs were defined as episodes that were either symptomatic or confirmed by a blood glucose measurement ≤70 mg/dL (≤3.9 mmol/L) with or without symptoms, that did not require medical attention (such as needing to call an ambulance, or a visit to the emergency room/hospital) or require help from anyone else to help manage the hypoglycemic event (such as needing help with getting something to eat or drink because they were not able to do it themselves). Night-time NSHEs were defined as occurring while the patient was asleep (after they had gone to bed until they became active the next day). Daytime NSHEs were defined as occurring while the patient was awake. After entering their demographic information, respondents were asked questions on the frequency, cause, duration and impact of NSHEs. The survey included validation controls; for example, minimum–maximum plausible values for each question and skip-pattern analysis based on responses to previous questions. Respondents were remunerated for their time if the questionnaire was completed.

Survey sample

Survey respondents were required to have a diagnosis of diabetes and to be aware of their diabetes type. All respondents had to be currently treated with insulin, were aged ≥20 years and were able to read Japanese. To reduce the effects of recall bias, respondents were required to have had at least one NSHE in the past 3 months. Recruitment of respondents was carried out through multiple online channels, such as website advertising, permission emailing and affiliate networks, to improve the generalizability of the results by avoiding the potential for bias from single-source recruitment. Several hundred websites were used as part of the recruitment drive. Respondents were not exposed to third-party advertising or direct marketing campaigns, nor were their data sold to third parties. Data obtained from the survey was used solely for research purposes. The panel was frequently refreshed to ensure that any changes in the online population that might be occurring were captured. Remuneration for participation in the survey was kept low to reduce the risk of incentivization bias. The selection process used a sampling frame in a pre-existing panel of persons with self-reported type 1 diabetes or type 2 diabetes. A convenience sample was used – there were no quotas for age, sex or type of diabetes. All respondents went through a healthcare profiler (screening questions) to ensure that their diabetes had been diagnosed by a physician, and that a relevant treatment was initiated. A stratified sampling procedure was employed using invitation selection criteria to account for disproportional response rates between stratification categories. Stratification variables were age (20–29, 30–39, 40–49, 50–59 and ≥60 years), diabetes type (type 1 diabetes and type 2 diabetes), sex and working status (working and non-working). The survey took place from 29 September to 3 October 2014.

Analysis strategy

Results are presented as frequencies or descriptive statistics (means and standard deviations). For questions on the impact of NSHEs on diabetes management, next day functioning and well-being, a response scale from 1 (e.g., 'Did not impact my ability to perform daily activities at all') to 7 (e.g., 'Prevented me from performing my daily activities') was used. A score of 4 corresponded with the answer 'Cannot say'. Responses rated 5–7 were summarized as 'yes,' indicating a negative impact resulting from the NSHEs.

All respondents provided informed consent to participate in the survey. Personally identifiable information was stored in a separate database from the respondents' answers and deleted once they were no longer required.

RESULTS

Respondent characteristics

A total of 411 (3,145 screened) respondents with self-reported diabetes who met the inclusion criteria (according to screening questions) completed the survey. The proportion of respondents working for pay was 64%. The mean (standard deviation) recall duration was 16.2 days (18.8 days) for daytime NSHEs and 18.9 days (17.7 days) for night-time NSHEs. The majority of the respondents were men (72%), with a mean age of 51 years (range 22–84 years). Diabetes type was split 44/56% for type 1 diabetes and type 2 diabetes, respectively. Mean body mass index was 25 kg/m^2 (5.0 kg/m^2; Table 1). Insulin alone or insulin in combination with diet and exercise was the regimen for 55% of respondents; all other respondents were treated with insulin in combination with other oral or injectable agents. The mean duration of diabetes was 15 years (9.6 years; range 0.3–50 years; Table 1). The proportion of all respondents experiencing a daytime NSHEs in the past 3 months was 92%. The proportion of all respondents reporting night-time NSHEs over the same period was lower at 44% (Table 1).

Characterization of the last NSHE

Daytime NSHEs

The mean number of daytime NSHEs in the past 3 months was 7.1 episodes (11.0 episodes). In patients with type 1 diabetes, 62% reported having experienced at least five daytime NSHEs in the past 3 months, and 45% reported at least 10

Table 1 | Respondent demographics and characteristics

	All	Type 1 diabetes mellitus	Type 2 diabetes mellitus
Sample size, n (%)	411 (100)	181 (44)	230 (56)
Mean age, years (SD)	51 (11.4)	41 (11.9)	55 (9.9)
Range (years)	22–84	22–84	28–80
Male, n (%)	297 (72)	111 (61)	186 (81)
BMI, kg/m² (SD)	25 (5.0)	23 (3.9)	26 (5.2)
Mean diabetes duration, years (SD)	15 (9.6)	15 (10.6)	15 (8.7)
Range	0.3–50	0.3–50	0.5–49
Mean no. medical complications (SD)	2 (0.9)	2 (0.9)	2 (0.9)
Range	1–5	1–4	1–5
Diabetes treatment, n (%)			
Insulin ± diet and exercise	91 (22)	59 (33)	32 (14)
Insulin + other oral/injectable agent	185 (45)	38 (21)	147 (64)
Insulin alone	135 (33)	84 (46)	51 (22)
Work for pay (yes), n (%)	261 (64)	113 (62)	148 (64)
Mean no. hours worked per week (SD)	34.2 (17.7)	33.9 (16.0)	34.4 (18.9)
Proportion of patients experiencing a daytime NSHE in the past 3 months, n (%)	377 (92)	171 (95)	206 (90)
Proportion of patients experiencing a night-time NSHE in the past 3 months, n (%)	181 (44)	104 (58)	77 (34)
Mean frequency of daytime NSHEs in past 3 months (SD)	7.1 (11.0)	11.1 (14.9)	3.9 (4.5)
Mean frequency of night-time NSHEs in past 3 months (SD)	1.9 (5.0)	3.2 (6.8)	1.0 (2.6)

BMI, body mass index; NSHE, non-severe hypoglycemic event; SD, standard deviation.

episodes over the same period. Patients with type 1 diabetes were also twice as likely to have had a daytime NSHE in the past week (50%) compared with type 2 diabetes (26%; Table 2). The mean duration of the most recent daytime NSHE was 43 min (55.8 min). Respondents took an average of 15 min (31.8 min) to realize that they were having a daytime NSHE. It took a further 12 min (67.2 min) for respondents to take action in relation to the daytime NSHE, and 1.7 h (6.4 h) for

respondents to feel that they were functioning at their usual level again. Overall, more than half of the NSHEs were recognized within 9 min, acted on within 9 min and were resolved within 39 min.

Night-time NSHEs
The mean number of night-time NSHEs in the past 3 months was 1.9 episodes (5.0 episodes). In patients with type 1

Table 2 | Diabetes management after last daytime non-severe hypoglycemic event

	All	Type 1 diabetes mellitus	Type 2 diabetes mellitus
Sample size with daytime NSHE in the past 3 months (n)	377	171	206
How long ago did last daytime NSHE occur?, n (%)			
<1 week ago	139 (37)	86 (50)	53 (26)
<2 weeks ago	53 (14)	21 (12)	32 (16)
<3 weeks ago	61 (16)	27 (16)	34 (17)
<4 weeks ago	48 (13)	15 (9)	33 (16)
4+ weeks ago	76 (20)	22 (13)	54 (26)
How was the last daytime NSHE recognized?, n (%)			
Symptomatic and confirmed by blood glucose testing	161 (43)	74 (43)	87 (42)
Symptomatic, but not confirmed by blood glucose testing	187 (50)	84 (49)	103 (50)
No symptoms, but confirmed by blood glucose on routine testing	29 (8)	13 (8)	16 (8)
Performed additional SMBG testing after last NSHE (yes), n (%)	215 (57)	89 (52)	128 (62)
Mean no. extra blood glucose tests in the 7 days after last NSHE (SD)	2.40 (3.5)	2.55 (3.7)	2.31 (3.3)
Contacted a healthcare professional after event (yes), n (%)	103 (29.7)	43 (26.9)	60 (32.1)
Did your last NSHE cause you to change your insulin dose?, n (%)	73 (19)	42 (25)	31 (15)
Mean duration of using changed insulin dose, days (SD)	2.7 (7.9)	1.4 (0.9)	5.1 (13.0)
Skipped/delayed next insulin dose after last NSHE (yes), n (%)	46 (12)	18 (11)	28 (14)

NSHE, non-severe hypoglycemic events; SD, standard deviation; SMBG, self-measured blood glucose.

diabetes, 20% of patients experienced at least 10 night-time NSHEs in the past 3 months. A large proportion (38%) of night-time NSHEs occurred between 12.00 and 02.00 hours, and a further 29% occurred between 02.00 and 04.00 hours. In 85% of cases, respondents were woken by the symptoms of hypoglycemia (Table 3). The mean duration of the last night-time NSHE was 51 min (56.6 min). Respondents took an average of 17 min (54.1 min) to realize they were having an NSHE after waking. It took 10 min (23.7 min) for respondents to take action, and 3.5 h (13.2 h) to feel as though they were functioning at their usual level again. Overall, as in daytime, more than half of night-time NSHEs were recognized within 9 min, acted on within 9 min and resolved within 39 min.

Impact of last NSHE on diabetes management
Daytime NSHE
In the 7 days after the last daytime NSHE, among those patients who reported increased blood glucose monitoring (57%), respondents carried out 2.40 (3.5) extra tests. Insulin dose was changed by 19% of respondents after their last daytime NSHE. The change in dose was maintained for an average of 2.7 days (7.9 days; Table 2). Subsequent to the daytime NSHE, 29.7% of respondents contacted a healthcare professional.

Night-time NSHE
In the week after the last night-time NSHE, among those patients who reported increased blood glucose monitoring (54%), the mean number of additional blood glucose tests carried out was 2.97 (4.3; Table 3). Insulin dose was changed by 16% of respondents. One-third (33.4%) of participants contacted a healthcare professional or doctor after their last night-time NSHE.

Impact of last NSHE on next day functioning and well-being
Daytime NSHE
The last daytime NSHE had a negative impact on 25% of respondents' ability to carry out their daily activities the following day (Table 4). The same proportion of respondents reported a negative impact on their work. A smaller proportion (6%) of respondents reported that their last daytime NSHE had caused them to be late for work/leave early or miss a full day. After their last daytime NSHE, 45% of respondents reported a fear of future hypoglycemic events (Table 4).

Night-time NSHE
The last night-time NSHE had a negative impact on sleep for 34% of respondents (Table 4). Specifically, returning to sleep was difficult for 22% of respondents. A similar proportion (23%) of respondents felt that their last NSHE had a negative effect on their next-day emotional state. Ability to carry our daily activities was adversely affected for 19% of respondents; however, fewer respondents reported a negative impact from their last night-time NSHE on work activities (10%). A small proportion of respondents (4%) were late for work, left early or missed a full day as a result of their last night-time NSHE. Subsequent to their last night-time NSHE, 55% of respondents expressed fear over further hypoglycemic episodes (Table 4).

DISCUSSION
The results of this survey confirm that NSHEs are not uncommon in people treated with insulin in Japan; occurring with a frequency of 7.1 and 1.9 events over a 3-month period for daytime and night-time NSHEs, respectively. The frequency of NSHEs was approximately threefold higher in patients with type 1 diabetes compared with type 2 diabetes, concurring with the findings of the United Kingdom Hypoglycemia Study Group[4].

Despite the common perception that NSHEs are of limited clinical importance, both daytime and night-time NSHEs had a significant impact on diabetes management and daily functioning. This observation is in agreement with previously published international surveys, suggesting that the burden of NSHEs is an artefact of hypoglycemia and not culturally determined[11]. In particular, NSHEs have a detrimental effect on patients' quality of life, hindering their ability to carry out usual activities. There are also strong emotional repercussions from NSHE, with patients reporting fear of future hypoglycemia. Additionally, night-time NSHEs directly compromise patients' quality of sleep. This is a concern, because disruption to sleep has been associated with metabolic abnormalities that can increase the risk of future hypoglycemic episodes, creating a vicious cycle[12,13].

The recovery phase of an NSHE prolongs the impact for several days. In total, 19% of respondents in the present study modified their insulin dose during the 7 days after an NSHE – a value slightly higher than has been reported in other countries using a similar survey (15.8%)[11]. Altering, and in particular decreasing, insulin dose might have negative consequences for glycemic control. It warrants mentioning that changes in insulin dose that are made according to discussions with healthcare professionals, and those made through a patient's own judgement, cannot be assumed to be equivalent in their effects on glycemic control and the risk of hypoglycemia. The effect of NSHE-related insulin dose alterations on glycated hemoglobin is beyond the scope of the present study, but should be the subject of further study given the potential clinical impact.

The results of this survey suggest that NSHEs lead to increased direct healthcare expenditure as a consequence of additional self-measured blood glucose test strip usage and unplanned visits to see healthcare professionals/physicians. However, respondents in this Japanese survey undertook slightly fewer additional self-measured blood glucose tests (2.95) in the 7 days after a night-time NSHE compared with respondents in other countries (3.6)[11].

Both daytime and night-time NSHEs reduced patients' capacity to carry out work activities, but this was more

Table 3 | Diabetes management after last night-time non-severe hypoglycemic event

	All (Type 1 diabetes mellitus and Type 2 diabetes mellitus)	Type 1 diabetes mellitus	Type 2 diabetes mellitus
Sample size with NSHE in the past 3 months (*n*)	181	104	77
How long ago did last NSHE occur, *n* (%)			
<1 week ago	32 (18)	21 (20)	11 (14)
<2 weeks ago	45 (25)	28 (27)	17 (22)
<3 weeks ago	38 (21)	21 (20)	17 (22)
<4 weeks ago	18 (10)	10 (10)	8 (10)
4+ weeks ago	48 (27)	24 (23)	24 (31)
What time did the NSHE occur?, *n* (%)			
Before midnight	26 (16)	12 (12)	14 (20)
Midnight to before 2 AM	64 (38)	37 (38)	27 (39)
2 AM to before 4 AM	49 (29)	27 (28)	22 (32)
4 AM to before 6 AM	23 (14)	18 (18)	5 (7)
After 6 AM	5 (3)	4 (4)	1 (1)
Situation when last night-time NSHE occurred, *n* (%)			
My hypoglycemia symptoms woke me up	154 (85)	91 (88)	63 (82)
I had no symptoms and did not wake up during the hypo, but I thought I had a hypo during the nights because of the way I felt when I woke up	14 (8)	6 (6)	8 (10)
I had hypoglycemic symptoms and my bed partner or someone else in my household woke me up	10 (6)	7 (7)	3 (4)
I regularly wake up to check my blood glucose during the night (even when not having hypoglycemic symptoms), and the reading was low	3 (2)	0 (0)	3 (4)
How was the last night-time NSHE recognized?, *n* (%)			
Symptomatic and confirmed by blood glucose testing	91 (50)	52 (50)	39 (51)
Symptomatic, but not confirmed by blood glucose testing	83 (46)	47 (45)	36 (47)
No symptoms, but confirmed by blood glucose on routine testing	7 (4)	5 (5)	2 (3)
Performed additional SMBG testing after last NSHE (yes), *n* (%)	98 (54)	54 (52)	44 (57)
Mean no. extra blood glucose tests in the 7 days after last NSHE (SD)	2.97 (4.3)	3.22 (4.4)	2.66 (4.2)
Contacted a healthcare professional after event (yes), *n* (%)	57 (33.4)	27 (27.9)	30 (41.6)
Did your last NSHE cause you to change your insulin dose? (yes), *n* (%)	28 (16)	19 (18)	9 (12)
Mean duration of using changed insulin dose, days (SD)	2.44 (3.3)	1.58 (1.2)	5.00 (6.1)
Skipped/delayed next insulin dose after last NSHE (yes), *n* (%)	13 (7)	7 (7)	6 (8)

NSHE, non-severe hypoglycemic events; SD, standard deviation; SMBG, self-measured blood glucose.

pronounced after a daytime NSHE, where 25% of patients reported a negative impact. A total of 10% of patients stated that their last night-time NSHE had at least some negative impact on their ability to carry out work activities, and 4% indicated that they 'Went to work late, left early or missed a full day' as a result.

In contrast to surveys carried out in other countries, NSHEs have a comparatively lower impact on work productivity and absenteeism in Japan[11]. We speculate that cultural differences in the acceptability of absenteeism might contribute to this observation. Conversely, 29.7% of Japanese patients visited a healthcare professional after a hypoglycemic episode compared with ~15% in other countries[11]. The decision to visit a healthcare professional instead of choosing self-management after an NSHE could also be due to cultural factors; however, the

increased number of interactions with healthcare professionals in Japan is likely to have significant cost implications that could exceed the potential savings made through reduced workplace absenteeism.

This survey was subject to several limitations. Foremost, the accuracy of reporting/influence of recall bias on the frequency of hypoglycemia is unknown, and could be significant given that the recall period was relatively long (up to 3 months). Although extensive efforts were made to ensure that a representative population was surveyed, selection bias might have been introduced through the use of internet administration of the survey (only patients who were computer-literate and had access to the internet could participate). Similarly, although remuneration for completing the questionnaire was low and unlikely to have influenced patients' decision to participate in

Table 4 | Impact of last NSHE on sleep (night-time only), next day functioning and well being

	All	Type 1 diabetes mellitus	Type 2 diabetes mellitus
Last daytime NSHE			
Negative impact of last NSHE on ability to carry out daily activities (yes), n (%)	95 (25)	50 (29)	45 (22)
Impact on work of NSHEs: Go to work late, leave early or miss full day (yes), n (%)	13 (6)	7 (7)	6 (5)
Impact on work of NSHEs: Miss a meeting/work appointment or fail to finish a task (yes), n (%)	20 (8)	10 (10)	10 (8)
Negative impact on ability to carry out work activities (yes), n (%)	59 (25)	34 (32)	25 (19)
Fear of having a daytime NSHE (yes), n (%)	186 (45)	91 (50)	95 (41)
Last night-time NSHE			
Did your last night-time NSHE have a negative effect on your sleep quality? (yes), n (%)	62 (34)	39 (37)	23 (30)
Did you have difficulty in returning to sleep after your last night-time NSHE? (yes), n (%)	36 (22)	21 (21)	15 (22)
Did your last night-time NSHE have a negative effect on your next day emotional state? (yes), n (%)	42 (23)	27 (26)	15 (20)
Did you last night-time NSHE have a negative effect on your ability to carry out daily activities? (yes), n (%)	35 (19)	18 (17)	17 (22)
Impact on work of NSHEs: Go to work late, leave early or miss full day (yes), n (%)	5 (4)	1 (2)	4 (7)
Impact on work of NSHEs: Miss a meeting/work appointment or fail to finish a task (yes), n (%)	2 (2)	2 (3)	0 (0)
Negative impact on ability to carry out work activities (yes), n (%)	12 (10)	6 (9)	6 (11)
Fear of having a night-time NSHE (yes), n (%)	227 (55)	110 (61)	117 (55)

NSHE, non-severe hypoglycemic events.

the survey, the potential for incentivization bias exists. It is also possible that some respondents misrepresented their diagnosis at screening. Only those who checked 'diabetes' continued through to the full survey, but we do not have reason to believe that the number of respondents misrepresenting their diagnosis would have been large enough to have had a significant impact on the findings. Self-reporting of diabetes type might not always be accurate, because a small number of patients with type 2 diabetes who start insulin immediately after diagnosis could mistakenly believe they have type 1 diabetes.

Prospective studies are required to explore the impact of reducing NSHEs on patients' treatment satisfaction and quality of life, including mental stress. Randomized controlled trials with a concurrent control would be preferable, but more flexible designs, such as delayed start trials, could also be acceptable. Future studies should also investigate the effect of diabetes duration on the impact of NSHEs on patients' diabetes management and daily functioning, particularly given the association between diabetes duration and hypoglycemia unawareness[14].

This survey is one of the first to show that, in a Japanese population, NSHEs have a strong, negative impact on patients' daily lives and their diabetes management, with wider economic consequences for patients and society. These findings are in concordance with previous international surveys, which suggests that the negative impact of NSHEs is consistent across cultures. The present study also confirms the need to move away from considering these events as minor or non-severe and to elevate their importance in the treatment of diabetes at all levels of healthcare provision.

ACKNOWLEDGMENT

DISCLOSURE

REFERENCES
1. Seaquist ER, Anderson J, Childs B, et al. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes

Association and the Endocrine Society. *Diabetes Care* 2013; 36: 1384–1395.

2. Pramming S, Thorsteinsson B, Bendtson I, *et al.* Symptomatic hypoglycaemia in 411 type 1 diabetic patients. *Diabet Med* 1991; 8: 217–222.

3. Donnelly LA, Morris AD, Frier BM, *et al.* Frequency and predictors of hypoglycaemia in type 1 and insulin-treated type 2 diabetes: a population-based study. *Diabet Med* 2005; 22: 749–755.

4. UK Hypoglycaemia Study Group. Risk of hypoglycaemia in types 1 and 2 diabetes: effects of treatment modalities and their duration. *Diabetologia* 2007; 50: 1140–1147.

5. Leiter LA, Yale J, Chiasson J, *et al.* Assessment of the impact of fear of hypoglycemic episodes on glycemic and hypoglycemia management. *Can J Diabetes* 2005; 29: 186–192.

6. Brod M, Christensen T, Thomsen TL, *et al.* The impact of non-severe hypoglycemic events on work productivity and diabetes management. *Value Health* 2011; 14: 665–671.

7. Leiter LA, Boras D, Woo VC. Dosing irregularities and self-treated hypoglycemia in type 2 diabetes: results from the Canadian cohort of an international survey of patients and healthcare professionals. *Can J Diabetes* 2014; 38: 38–44.

8. Sreenan S, Andersen M, Thorsted BL, *et al.* Increased risk of severe hypoglycemic events with increasing frequency of non-severe hypoglycemic events in patients with type 1 and type 2 diabetes. *Diabetes Ther* 2014; 5: 447–458.

9. Levy AR, Christensen TL, Johnson JA. Utility values for symptomatic non-severe hypoglycaemia elicited from persons with and without diabetes in Canada and the United Kingdom. *Health Qual Life Outcomes* 2008; 6: 73.

10. Brod M, Pohlman B, Wolden M, *et al.* Non-severe nocturnal hypoglycemic events: experience and impacts on patient functioning and well-being. *Qual Life Res* 2013; 22: 997–1004.

11. Brod M, Wolden M, Christensen T, *et al.* A nine country study of the burden of non-severe nocturnal hypoglycaemic events on diabetes management and daily function. *Diabetes Obes Metab* 2013; 15: 546–557.

12. Nedeltcheva AV, Kessler L, Imperial J, *et al.* Exposure to recurrent sleep restriction in the setting of high caloric intake and physical inactivity results in increased insulin resistance and reduced glucose tolerance. *J Clin Endocrinol Metab* 2009; 94: 3242–3250.

13. Buxton OM, Pavlova M, Reid EW, *et al.* Sleep restriction for 1 week reduces insulin sensitivity in healthy men. *Diabetes* 2010; 59: 2126–2133.

14. Smith CB, Choudhary P, Pernet A. Hypoglycemia unawareness is associated with reduced adherence to therapeutic decisions in patients with type 1 diabetes: evidence from a clinical audit. *Diabetes Care* 2009; 32: 1196–1198.