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## Understanding the Economic Burden of Nonsevere Nocturnal Hypoglycemic Events: Impact on Work Productivity, Disease Management, and Resource Utilization

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### ABSTRACT

**Objective:** Nonsevere hypoglycemic events are common and may occur in one-third of persons with diabetes as often as several times a week. This study's objective was to examine the economic burden of nonsevere nocturnal hypoglycemic events (NSNHEs). **Methods:** A 20-minute Web-based survey, with items derived from the literature, expert input, and patient interviews, assessing the impact of NSNHEs was administered in nine countries to 18 years and older patients with self-reported diabetes having an NSNHE in the past month. **Results:** A total of 20,212 persons were screened, with 2,108 respondents meeting criteria and included in the analysis sample. The cost of lost work productivity per NSNHE was estimated to be between \$10.21 (Germany) and \$28.13 (the United Kingdom), representing 3.3 to 7.5 hours of lost work time per event. A reduction in work productivity (presenteeism) was also reported. Compared with respondents' usual blood sugar monitoring practice, on average,  $3.6 \pm 6.6$  extra tests were

conducted in the week following the event at a cost of approximately \$87.1 per year. Additional costs were also incurred for doctor visits as well as medical care required because of falls or injuries incurred during the NSNHE for an annual cost of \$2,111.3 per person per year. When taking into consideration the multiple impacts of NSNHEs for the total sample and the frequency that these events occur, the resulting total annual economic burden was \$288,000 or \$127 per person per event. **Conclusions:** NSNHEs have serious consequences for patients. Greater attention to treatments that reduce NSNHEs can have a major impact on reducing the economic burden of diabetes. **Keywords:** economic burden, nocturnal hypoglycemia, resource utilization, work productivity.

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### Introduction

Nonsevere hypoglycemic events are common in both type 1 and type 2 diabetes and may occur in approximately one-third of persons with diabetes, with frequency of events as often as several times a week [1]. These events can occur at any time of day or night while patients are at rest or engaged in activities [1–3]. These events represent a major challenge for both patients and clinicians, interfere with optimal long-term diabetes control, and contribute to excess morbidity and mortality [4–6]. In addition, nonsevere hypoglycemia has been shown to have an economic burden for patients, employers and health care payer systems [7], increased blood glucose (BG) monitoring, health care resource utilization, and patient out-of-pocket expenses [7,8].

In previous survey studies of both nighttime and daytime events, nonsevere nocturnal hypoglycemic events (NSNHEs), those occurring while sleeping, have been shown to potentially have a greater impact than daytime events on lost work productivity due to both absenteeism and presenteeism [7]. Furthermore, qualitative research has shown that nighttime events disrupt both sleep quality and quantity, resulting in impaired functioning and well-being the following day [8]. Thus, previous quantitative as well as qualitative research on NSNHEs has begun

to suggest that these events are consequential contributors to increasing health care costs as well as the overall economic burden of diabetes [3,7,8]. The purpose of this study was to explore, in greater depth than has previously been done, the economic burden of these NSNHEs in terms of lost work productivity and health care resource utilization. This information is critical data that can be instrumental in helping to better understand, manage, and contain costs associated with these events and reduce the overall cost of care.

### Methods

#### Survey Development and Conduct

A survey assessing the impact of NSNHEs was developed on the basis of the literature, expert input, and interviews with 78 persons with diabetes in nine focus groups in four countries (the United States, the United Kingdom, Germany, and France) who recently had experienced an NSNHE [8]. The survey items were developed on the basis of 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

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same eligibility criteria as the focus groups. These steps were conducted 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 questionnaire was translated into all relevant languages by using a forward and backward translation process [8]. The survey was administered via a secure Internet server in the United States, the United Kingdom, Germany, Canada, France, Italy, Spain, The Netherlands, and Sweden. Findings, based on the current survey regarding the impact of NSNHEs on daily functioning and diabetes management, have been previously published [9].

NSNHEs were defined for the respondent as “nighttime hypoglycemic episode that happened while you were sleeping and did not require medical attention (such as needing to call an ambulance, go to the emergency room/hospital) or did not require help from anyone else to manage the hypo. You knew that you were having this hypoglycemic episode because you had symptoms like sweating and/or confusion or perhaps you experienced no symptoms, but noted the hypoglycemic episode when measuring your blood sugar.” Respondents were asked questions regarding reasons for the event, length of time of the event, impact on productivity, daily functioning, and well-being. The survey took approximately 20 minutes to complete, and respondents were remunerated US \$3 to US \$5 depending on country for completing the survey. The survey had several real-time validation steps (e.g., plausible min–max input values) and skip-patterns depending on the respondents’ reply. Before database release, additional cross-checks were performed.

### Sample

To be eligible to complete the survey, the respondent had to have a self-reported diagnosis of diabetes and experienced at least one NSNHE in the past month, be 18 years or older, and able to read the predominant language of the country he or she was living in. To ensure the generalizability of the results and reduce recruitment source bias, a multisource informant strategy was used. A multisource informant strategy is important when conducting correlational/regression-oriented research because it allows one to examine associations between predictors and outcomes when common method or source variance is not shared and enables researchers to rule out alternative explanations that would probably not be testable with single-source, single-method data sets [10,11]. The multisource informant strategy included a preconsented, online patient panel, e-mail recruitment, affiliate networks, and Web site advertising. Patients were recruited from more than 100 Web sites as well as from face-to-face and telephone surveys where appropriate to include members who were not frequent online users. Furthermore, all respondents were blinded to the purpose of the survey before entering the survey to reduce the possibility of self-identifying as a person with diabetes for the purpose of completing the survey. All respondents had either been identified as a person with diabetes and age 18 years or older in a prior blinded survey as a prerequisite of being a panel member (not related to this study) or, if not a member of the panel, by answering a blinded question asking about all their diagnoses and then being invited to enter the survey only if diabetes was listed as a diagnosis. In addition, the panel was constituted to be representative of the general population for age, sex, race, and income, and used for research only; panelists were not exposed to third-party advertising or direct marketing campaigns, nor were their personal data sold to third parties. The panel was also frequently refreshed to ensure that the panel was dynamic in nature and reflected any changes in the online population that might be occurring. Last, the incentive was low (~US \$3–\$5 depending on country) to help ensure that there was no undue incentive to participate in the

panel. The incentive amount was set by the survey administrators on the basis of the length of the survey and historical knowledge of respondent expectations, and was consistent with honoraria given for similar surveys. Because of ethical considerations, the same honorarium was given to both panel and nonpanel respondents. For panel members, the honorarium was given as a “credit” that could be combined with “credits” from other surveys and redeemed at a later point in time.

The selection process used a sampling frame in a preexisting panel of persons with self-reported type 1 or type 2 diabetes. All respondents went through a health care profiler (screening questions) to ensure that a physician had diagnosed their diabetes and that a relevant treatment was initiated. A stratified sampling procedure used invitation selection criteria to account for disproportional response rates between stratification categories. Stratification variables were age (18–29 years, 30–49 years, 50–64 years, and  $\geq 65$  years), diabetes type (type 1 diabetes and type 2 diabetes), sex, and working status (working and nonworking).

### Statistical Testing

Results by country are presented via frequencies or descriptives (means and SDs) with differences explored by using analysis of variance for continuous variables and Pearson chi-square for proportions. Statistical significance was tested between countries with the highest and lowest values. Responses for amount of work time lost contained outliers ( $> 180$  hours), or observations that appeared to be inconsistent with other observations in the data set. To account for these departures from normality, a 5% trim was used [12]. This trim was used for the analysis for calculating the cost of lost work productivity and resulted in two cases being dropped. The human capital approach using average wages to estimate productivity was used. To estimate input for the human capital method, an average of 36.8 working hours per week (corresponding to the self-reported working hours in Table 1) with an estimated 47 working weeks per year (a total of 1730 working hours per year) was used. The 2011 gross domestic product per capita was used as an estimate for annual income [13]. An estimated average income (in US \$) of \$29.79/h in the United States, \$22.25/h in the United Kingdom, \$23.34/h in Germany, \$24.98/h in Canada, \$21.64/h in France, \$18.78/h in Italy, \$18.84/h in Spain, \$25.96/h in The Netherlands, and \$24.86/h in Sweden was used to estimate the value of the lost productivity [13]. The estimated productivity loss per NSNHE because of absenteeism was calculated on the basis of the proportion of persons reporting missed work multiplied with the hourly income multiplied with the hours missed (e.g., for an NSNHE during working hours in the United States, 12.6% of the sample reported missing work for 3.5 hours at the cost of \$29.79/h, which is approximately equal to \$13.37 per event).

The costs for doctor visits (or other health care professional) were derived from in-country data (Spain [14], Italy [15], France [16], The Netherlands [17], Sweden [18], the United Kingdom [19], the United States [20], Canada [20], and Germany [21,22]). The costs were converted into US \$ by using the International Monetary Fund exchange rate data on June 1, 2012 [23]. The costs per visit used to estimate the value of general practitioner visits were \$40.66 (Spain), \$28.34 (Italy), \$28.34 (France), \$34.50 (The Netherlands), \$164.72 (Sweden), \$47.50 (the United Kingdom), \$65.51 (the United States), \$65.51 (Canada), and \$38.20 (Germany).

Presenteeism was assessed by using the Endicott Work Productivity Scale [24] as well as a patient-reported Likert scale assessment. The Endicott Work Productivity Scale is a 25-item measure assessing the impact of a disease/event on a person’s ability to perform work functions due to behaviors and subjective feelings or attitudes (e.g., ability to concentrate or impatience or

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