Participatory Surveillance of Hypoglycemia and Harms in an Online Social Network

Elissa R. Weitzman, ScD, MSc; Skyler Kelemen, BA; Maryanne Quinn, MD, MPH; Emma M. Eggleston, MD, MPH; Kenneth D. Mandl, MD, MPH

Importance: Surveillance systems for elucidating the burden of hypoglycemia are limited.

Objective: To quantify experiences of hypoglycemia and related harms, members of an international online diabetes social network with insulin-dependent diabetes mellitus were polled through a software application (“app”). Aggregate results were returned to participants through network channels.

Design: The study period was from March 2011 through April 2012, during which time retrospective reports about experiences with hypoglycemia and related harms were collected from participants using the app.

Setting: The study was undertaken within the TuDiabetes.org international online diabetes social network.

Participants: Eligibility criteria included TuDiabetes membership, age 13 years or older, a self-reported diagnosis of diabetes mellitus, ability to read and write English, and Internet access. Of 2827 app users, 687 (response rate, 24.3%) opted in to the volunteer sample.

Main Outcome Measures: Primary outcomes included the following: frequency of “going low” (having a low glucose value in the past 2 weeks) and episodes of severe hypoglycemia (in the past 12 months), and, for respondents reporting recent and/or severe hypoglycemia, lifetime experience of vehicle crashes or severe medical injury, daily debilitating worry, and withdrawal from driving, exercise, sex, and going outside of the home to avoid hypoglycemia and consequences. Secondary outcomes included measures of research engagement.

Results: Of 613 respondents (24.3% of app users), 49.1% reported more than 4 episodes of “going low” in the past 2 weeks and 29.2% reported 1 or more severe low in the past year; 16.6% reported both more than 4 recent low episodes and 1 or more severe event in the past year. Harms were common, including daily debilitating worry (45.8%), vehicle crash or injury (15.0%), and withdrawal from exercise, driving, leaving home, and having sex (54.0%, 37.4%, 24.8%, and 22.7%, respectively). Of all respondents, 54.2% reported multiple harms, the risks for which were highest (73.7%) among respondents with a past-year severe event (odds ratio, 2.39; 95% CI, 1.60-3.58; P < .001 controlling for frequent recent low episodes and demographic and disease factors). Engagement was high, with 96.6% of the sample permitting recontact for research and 31.7% posting personal study data on their app profile page; 40.5% of 2825 unique page views of research-related materials published on the community site involved views of returned research results.

Conclusions and Relevance: Participatory surveillance of hypoglycemia in an online diabetes social network enables characterization of patient-centered harms in a community sample and bidirectional communication with affected persons, augmenting traditional surveillance.


Hypoglycemia is a serious sequel of diabetes treatment not consistently tracked by formal health surveillance. Associated harms span vehicle crashes (car, truck, bicycle, or other) and injuries, missed work, debilitating worry, medical complications, and death. Insulin is the second most commonly prescribed drug associated with serious adverse drug reports made to the US Food and Drug Administration (FDA). Insulin-associated hypoglycemia accounts for one-third of all US emergency department visits related to medication use by older adults. Despite
insulin’s widespread use and the magnitude of hypoglycemia-related harms, monitoring of hypoglycemia has been limited to emergency department visit surveillance or adverse event reporting in clinical trials.11,12 Reports about events below the threshold for an emergency department visit and reports from community-based patient samples are lacking.

Pogach and Aron13 call for improved surveillance of hypoglycemia by the Centers for Disease Control and Prevention (CDC) and the FDA. Current CDC surveillance assets such as the Behavioral Risk Factor Surveillance System and the National Health and Nutrition Examination Study do not acquire information specific enough to advance this goal nor use suitably targeted sampling frames; moreover, traditional use of landline-based telephone systems to contact potential study subjects to participate in health interviews now misses important populations.14,15 Voluntary drug problem reporting to the FDA by pharmacists, physicians, and consumers provides some insight into the occurrence of hypoglycemia but is greatly underused.16,17 Reports triggered by scanning electronic health records may augment monitoring but lack specificity.18 Furthermore, standard surveillance approaches are directed toward the patient only and lack channels for patients’ feedback and opportunities to collaborate with them to elucidate and quantify patient-centered outcomes.

Dynamic engagement of online communities may augment standard surveillance.19-21 Patients with chronic illnesses increasingly gather in online communities (eg, http://www.patientslikeme.com, http://www.dlife.com, http://www.curetogether.com). Large “self-organizing” cohorts of patients uniquely positioned to describe their health care, experiences, to randomized trials.30 While participatory engagement produces results comparable, in some circumstances, to randomized trials.30 While participatory surveillance of distributed online populations cannot provide generalizable, denominator-based rates, it can characterize risk within online communities using a bidirectional communication channel that enables repolling, feedback, and even rapid-cycle intervention.

We engaged an online diabetes social network in participatory surveillance to measure hypoglycemia-related patient-centered outcomes. Building on prior work engaging this community,31 we used a closed-loop approach of polling and feeding back results through network channels. We quantified both recent and past-year severe hypoglycemia, testing for elevated risks for harms. We sought to understand harms among persons reporting severe hypoglycemia in the past year, a group that may be identified in standard reporting systems as “at risk” for problems. We also assessed harms among persons reporting frequent recent, but not necessarily severe, hypoglycemia, who may not be identified as at risk by traditional surveillance but whose experience of harms may be substantial. Secondary outcomes included measures of community engagement with the research.

METHODS

SETTING

We collected structured self-reports of hypoglycemia and related harms using a software application (“app”) called TuAnalyze, which supports privacy-preserving participatory surveillance by members of the TuDiabetes.org international online diabetes social network.22,31 TuDiabetes has more than 25,000 members; 77% reside in the United States, 62% are female, and 72% have either type 1 diabetes mellitus (T1D) or latent autoimmune diabetes in adults (LADA). The median member age is 41 years. TuAnalyze is freely available to TuDiabetes members.2 The app reinforces participation through contextualized feedback of maps and graphs of user-reported glycated hemoglobin (HbA1c) values. Summary data from member surveys are returned to the community through a site research blog (the main dissemination vehicle) and through newsletters and postings on the site home page. Consent is obtained within the app for use of member data. Study activities were approved by the Boston Children’s Hospital institutional review board. Neither TuDiabetes nor study investigators have any commercial interest in TuAnalyze.

SAMPLE ELIGIBILITY AND PARTICIPATION

Eligibility criteria include TuDiabetes membership, age 13 years or older, a self-reported diagnosis of diabetes mellitus, ability to read and write English, and Internet access. Persons using the app as a proxy for another person, such as family members (n=74), were excluded from analyses. During the study period of March 2011 through April 2012, 687 of 2827 app users (response rate, 24.3%) took 2 complementary surveys about hypoglycemia and diabetes care using the app (Figure, A). Compared with all TuDiabetes members, TuAnalyze survey respondents were more likely to reside in the United States (86% vs 77% [odds ratio, 1.85; 95% CI, 1.48-2.30]; P<.001), have T1D/LADA (80% vs 72% [odds ratio, 1.56; 95% CI, 1.28-1.90]; P<.001), and were older on average (44 years vs 42 years; P<.001). There was no difference in the sex makeup of survey and source populations. Of the 687 respondents, 613 (89%) reported using insulin and comprise the final sample. Respondents who entered survey data before and after feedback of summary survey data on the site research blog (47% and 53%, respectively) did not differ in age, sex, or type.

SOURCES OF DATA

Information about recent and severe hypoglycemia, associated harms, disease, and demographic and health care characteristics were collected from respondents using the app. Data about community engagement with the research included the following: (1) total unique page views for the TuAnalyze research blog used to report summary statistics about the frequency of recent hypoglycemia, severe hypoglycemia, and related harms generated from TuAnalyze surveys (tallied using Google analytics for March 2011 through March 2012); (2) the proportion of users permitting recontact through the app for ongoing research; and (3) the proportion of users opting to display on their social network profile page their most recent HbA1c value entered through the app. An export of current TuDiabetes member profile information was obtained from site administrators for analyses of response bias; privacy protections within the app precluded identification and exclusion of TuAnalyze survey respondents from the member list for comparisons of survey and source populations.
MEASURES

Frequency of Recent and Severe Hypoglycemia

Survey respondents reported “recent lows” (low glucose values) as the number of times they had “gone low” in the past 2 weeks. No specific definition for going low was offered in this context, since the goal was to elicit patient-defined episodes of hypoglycemia. Severe hypoglycemia was assessed separately, as the number of occasions in the past 12 months when survey respondents experienced a low blood glucose level resulting in their becoming unconscious, seizing, or requiring glucagon, medical treatment, and/or help from another person to treat the hypoglycemia. This definition is consistent with other published reports of conditions for serious or severe hypoglycemia.32 Because of the nonnormal distribution of these 2 measures, we dichotomized them at the median value into groupings of more than 4 or fewer for “recent lows” and 1 or more or none for “severe lows.”

Hypoglycemia Unawareness

Respondents were asked to report on hypoglycemia unawareness, defined in the survey as the absence of the typical early signs and symptoms of low blood glucose level. Respondents who reported being unsure about their hypoglycemia unawareness (5% of the sample) were classified as hypoaware for analyses. In addition, participants reported on the blood glucose value range at which they typically first start to feel their blood glucose level is “low.” These values were reported in 10-unit increments, from “below 40 mg/dL” to “100 mg/dL or higher” (to calculate as millimoles per liter, multiply by 0.0555).

Disease and Demographic Characteristics

TuAnalyze users indicated their diabetes type as T1D/LADA, type 2 diabetes mellitus (T2D), prediabetes, or gestational diabetes. No insulin-using respondents reported gestational or prediabetes, and therefore none were included in the final sample for these analyses. We dichotomized diabetes type into T1D/LADA and T2D, based on underlying disease mechanism. Self-reported values of HbA1c were collected through the app as described elsewhere31; consistent with American Diabetes Association (ADA) standards,33 respondents with a most recent HbA1c value of 7% or higher were classified as “above target” compared with those with values lower than 7% (7.5% was used for respondents younger than 19 years). Respondents identifying solely as white and non-Hispanic were classified as white. Age was dichotomized at the median of 44 years and diabetes duration at the median of 17 years.

Adherence With Recommended Care

Adherence with clinical practice recommendations was defined as receiving all five 2012 ADA clinical practice recommendations: any history of a pneumonia vaccination, and past-year history of an influenza vaccination, dilated eye examination, foot examination, and lipid profile.33 Self-care measures included typical frequency of self-monitoring of blood glucose (SMBG), dichotomized at the ADA minimum recommendation of 3 or more times per day, and 4 or more visits with a diabetes clinician in the past year.

Harms Attributed to Hypoglycemia

Participants reported on the following: experiencing a vehicle crash or severe injury in their lifetime, worry affecting their daily...
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### EXPERIENCE AND CORRELATES OF HYPOGLYCEMIA IN THE SAMPLE

Reported number of recent lows ranged from 0 to 75, with a median of 4 and a mean of 6.2. More than half (53.2%) of those with T1D/LADA and 18.2% of those with T2D reported experiencing more than 4 lows in the past 2 weeks. Only 9% of the sample reported no lows in the past 2 weeks. Severe lows in the past 12 months were less common, with 70.8% of the sample reporting none and at least 1 severe event. The median blood

### DATA ANALYSES

We used χ² tests and the 2-sample t test for analyses of response bias. Demographic correlates and harms associated with hypoglycemia were identified using logistic regression. Odds for harms were calculated among respondents reporting frequent recent and severe lows, using multivariate logistic regression. Using a propensity score approach, we predicted each respondent’s probability of experiencing frequent recent or past-year severe lows, controlling for effects of significant bivariate correlates, including sex, race (white or other), age (continuous), disease duration (continuous), diabetes type (T1D/LADA or T2D), hypoglycemia unawareness, SMBG (≥5 times per day, or fewer), pump and/or continuous glucose monitor (CGM) use. Adjusted odds of harms related to recent lows were estimated controlling for the experience of severe lows, and vice versa, to characterize the effects on outcomes of each category of low. Analyses were conducted in SAS version 9.3 statistical software (SAS Institute Inc.).

### RESULTS

#### DEMOGRAPHIC CHARACTERISTICS OF THE SAMPLE

Of 613 respondents, the majority were white, located in the United States, and female. Most (88.3%) reported having T1D/LADA (Table 1). The age range of the sample was from 14 to 81 years (mean, 43 years; median, 44 years). Reported disease duration ranged from 0 to 67 years (mean, 19 years; median, 17 years). In their application settings, 96.6% of respondents permitted recontact by the research team and 31.7% chose to have their HbA1c value entered in the application displayed on their TuDiabetes profile page.
glucose value at which respondents reported typically experiencing the first symptoms of hypoglycemia was 60 to 69 mg/dL, reported by almost one-third of respondents (32.3%). Nearly three-quarters of participants (73.2%) reported first feeling low at values between 50 and 79 mg/dL.

In bivariate analyses, experiencing more than 4 recent lows was associated with female sex, younger age, T1D/LADA, insulin pump and/or CGM use, longer disease duration, an HbA1c value under 7%, high daily SMBG, and dissatisfaction with diabetes health care; experiencing severe hypoglycemia in the past year was associated with female sex, CGM use, longer disease length, an HbA1c value higher than 7%, hypoglycemia unawareness, and cost barriers to care (Table 1). A small percentage of respondents (9.6%) did not report an HbA1c value through the application; compared with respondents who had entered an HbA1c value, this group was less likely to report high daily SMBG and more likely to report cost barriers to care, but did not differ on other measures.

**HYPOGLYCEMIA-RELATED HARMs**

Harms from hypoglycemia were common (Table 2). The most frequently reported harm in the total sample was avoiding exercise, reported by 54.0% of respondents, followed by daily debilitating worry about hypoglycemia, which was reported by 45.8%. These harms were also the most common among those reporting more than 4 recent lows or a past-year severe low. Fifteen percent of respondents reported having an accident or injury as a result of hypoglycemia—including 19.7% of those who reported frequent recent hypoglycemia and more than one-quarter (25.7%) of those reporting a past-year severe low. More than half (54.2%) of all respondents reported experiencing more than 1 of the assessed harms. Compared with respondents who did not report frequent recent lows, respondents reporting this were more likely to regularly limit their driving and sexual activity to avoid experiencing hypoglycemia and its consequences. Participants reporting at least 1 severe low in the past year were more likely than those who did not to report an accident or injury as a result of hypoglycemia, daily debilitating worry about hypoglycemia, and 3 of 4 assessed withdrawal behaviors. Experience of multiple harms was common among those experiencing frequent recent lows and severe lows (63.0% and 73.4%, respectively). Risks for multiple harms were highest among respondents with a past-year severe event, in analyses controlling for demographic, disease, and health care factors and experience of frequent recent hypoglycemia.

**ENGAGEMENT**

Almost all users (96.6%) opted to permit research re-contact. Approximately one-third of users (31.7%) opted to display their HbA1c value on their app profile page where persons authorized by them could see it. Of 2825 page views of study materials posted in the TuAnalyze research blog, 40.5% involved a review of interim research results (Figure, B). Engagement measures did not differ by experience of recent or severe hypoglycemia.

Using participatory surveillance, we quantified recent and severe hypoglycemia and patient-centered harms among members of an online international diabetes social network. Though our sample is not denominator based and cannot be used to estimate general population rates, reported hypoglycemia levels were similar to those found among carefully selected clinical cohorts: 36.7% of patients with T1D reported experiencing severe hypoglycemia in the past year in a large multicenter British-Danish clinical cohort22; 30.3% of T1D respondents in our sample reported this. In the Veterans Affairs Diabetes Trial of patients with T2D,16 17.6% of participants reported symptomatic (not necessarily severe) hypoglycemia; among 119 T2D TuAnalyze respondents using insulin or an oral agent, 22 (18.5%) reported severe hypoglycemia in the past year. Correlates were consistent with published reports and hypoglycemia was strongly associated with “hypoglycemia unawareness”37,38 and use of a CGM. The latter association likely reflects device use to control an established hypoglycemia risk.39-42 There was
no clear relationship between hypoglycemia and report of receiving helpful information about hypoglycemia from one’s physician or the social network, self-care patterns, health care interactions, or adherence with clinical practice recommendations. This may reflect limited influence of these factors on hypoglycemia occurrence or be an artifact of the self-selecting nature of the study sample.

Harms were especially evident among respondents reporting a severe event in the past year, among whom risks were elevated for 5 of 6 assessed harms. Daily debilitating worry and withdrawing from normal activities to avoid or mitigate the effects of hypoglycemia were common and may be driving quality of life down and productivity losses up among persons with diabetes—outcomes reported in large sample clinical and prospective cohort studies. A less common, but extremely serious, harm involves experiencing an accident or injury related to hypoglycemia.

Engagement was high—virtually all respondents opted in to research recontact and one-third shared personal research data with others via their TuDiabetes profile, using standard tools. Many respondents and network members reviewed research results, a proof of concept using standard tools. Many respondents and network research data with others via their TuDiabetes profile, in turn to research recontact and one-third shared personal experiences of an accident or injury related to hypoglycemia.

Patient engagement in disease-focused social networking is strong and growing, reflecting both the appeal of this organic and grassroots phenomenon and patients’ need for community, information, and support. Harnessing this engagement may enable population health monitoring and clinical care redesign through enabling collection of patient-reported data. Use of the inherently open and dynamic system to engage an online community sample in quantifying patient-centered measures may introduce bias related to the inherently opt-in model. Outcome estimates are not generalizable to nonnetwork populations nor network members who opt not to use TuAnalyze. Reported levels of type, device use, glycemic control, SMBG, and insurance among the study sample may differ from population-based comparator groups. This may be acceptable when the goal is rapid as opposed to nationally representative health surveillance and preservation of a feedback channel. Self-reports present a validity challenge, as in traditional monitoring. Standards for benchmarking engagement are lacking, as are measures of impact of returning research results on engagement and outcomes. Midstudy feedback to participants may influence subsequent reporting.

In conclusion, quantification of experiences of hypoglycemia and harms in an online diabetes social network enables characterization of serious patient-centered adverse outcomes using an approach that complements traditional surveillance and provides a communication channel back to affected participants. Establishing participatory surveillance and bidirectional communication among a motivated sample using appropriate safeguards for privacy, safety, and autonomy establishes a new toolkit for outcomes research. This may be a boon for monitoring and ameliorating diabetes.

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Author Affiliations: Children’s Hospital Informatics Program at the Harvard-MIT Division of Health Sciences and Technology (Drs Weitzman and Mandl and Ms Kelemen), Divisions of Adolescent Medicine (Dr Weitzman) and Emergency Medicine (Dr Mandl), Diabetes Program (Dr Quinn), and Manton Center for Orphan Disease Research (Dr Mandl), Boston Children’s Hospital, Boston, Massachusetts; Departments of Pediatrics (Drs Weitzman, Quinn, and Mandl) and Population Medicine (Dr Eggleston), Harvard Medical School, Boston; and Harvard Pilgrim Health Care Institute and Division of Endocrinology, Diabetes, and Hypertension, Brigham and Women’s Hospital, Boston (Dr Eggleston).

Correspondence: Elissa R. Weitzman, ScD, MSc, Children’s Hospital Informatics Program, One Autumn Street, Room 541, Boston, MA 02215 (elissa.weitzman@childrens.harvard.edu).

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