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The COVID-19 Hinterland: How the pandemic has affected chronic diabetes management in the United States

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ABSTRACT

Objective: This is first study of its kind to measure how, and to what extent, the pandemic has affected diabetes management in Americans with or without COVID-19.

Research Design and Methods: We conducted a cross-sectional investigation using data from the real-world, population-based iNPHORM study. Participants 18-90 years old, living in the US, diagnosed with type 1 or 2 diabetes, taking insulin and/or secretagogues were recruited from online panels of the general public. We examined the impact of the COVID-19 situation on socio-economic, behavioural/clinical, and psychosocial aspects of glycemic management.

Results: Data from 667 respondents (type 1 diabetes: 18%; type 2 diabetes: 82%) were analyzed. Almost 25% reported A1C values ≥8.1%. Rates of severe and non-severe hypoglycemia were 0.68 (95%CI: 0.5-0.96) and 2.75 (95%CI: 2.4-3.1) events per-person month, respectively. Ten respondents reported a confirmed or probable COVID-19 diagnosis. Because of the pandemic, 20-28% of respondents experienced difficulties affording housing, sufficient food to avoid hypoglycemia, and diabetes therapies/testing strips. Over one-quarter reported issues retrieving antihyperglycemics from the

pharmacy and over one-third reported challenges consulting with diabetes providers. The pandemic contributed to therapeutic non-adherence (14%), drug rationing (17%), and reduced monitoring (16%). Many struggled to keep track, and in control, of hypoglycemia (12-15%) and lacked social support to help manage their risk (19%). Nearly half reported decreased physical activity. Few differences emerged by diabetes type.

Conclusions: The results of this study can inform decisive action to re-stabilize routine diabetes management amidst the pandemic, helping to protect the health of America's vulnerable populations.

Strengths and limitations of this study

- This is the first and most comprehensive investigation to quantify the impact of the COVID-19 situation on the socio-economic, behavioural/clinical, and psychosocial aspects of glycemic management in US outpatient communities.

- We developed a novel pandemic-specific questionnaire that was administered online to a large, real-world cohort of Americans with type 1 and type 2 diabetes taking insulin and/or secretagogues.
- Estimates presented in our study may be conservative as they describe the early phase of the pandemic.

COVID-19 is among the most devastating health crises in American history. The first reported infection in the United States (US) occurred on January 19th, 2020 (1). Since then, the number of confirmed US-cases has surpassed 22.4 million, including over 374,000 deaths (2).

People with diabetes (PWD) have been identified as clinically vulnerable to COVID-19. In the US, diabetes ranks as the second most common underlying health condition among all cases and has been connected to more severe infection (3,4). However, less appreciated in the literature are the disruptions caused by the pandemic on routine diabetes care. These disruptions expose not only those with COVID-19, but all 34+ million Americans with diabetes to poor outcomes. Understanding how the pandemic

affects diabetes services and management is crucial to informing short- and long-term clinical decision-making and public health planning. Targeted measures to help protect these Americans from the direct and indirect effects of the COVID-19 pandemic should be a top priority for all healthcare and government officials.

The complex hinterland of COVID-19 and diabetes

The pathophysiological benefits of glycemic control on diabetes outcomes have been well-established. Numerous studies have linked chronic hyperglycemia and glycemic variability to increased risks of micro- and macro-vascular complications and mortality. In addition, dysglycemia can potentiate immunosuppression (5), increasing viral susceptibility and risk of poor clinical outcomes (6). While the role of coexistent diabetes in the pathogenesis of COVID-19 is still being determined (7), emerging signals suggest that euglycemia protects against infection and severity of prognoses (8,9). These data are consistent with evidence from other viral infections where glucose control showed to augment host immune response (5,10).

To mitigate COVID-19 risks, several national and international organizations have published diabetes pandemic guides, urging PWD to maintain scrupulous adherence to all self-management and public health recommendations (7,8). Notably, the Centers for Disease Control and Prevention (CDC) (11) has recommended maintaining at least a 30-day supply of medication and 2-week supply of food. The American Diabetes Association (ADA) (12) has advised storing blood glucose (BG) emergency supplies (i.e., glucagon and ketone strips). And the International Diabetes Federation (13) has encouraged healthy nutrition and regular monitoring to help avoid the complications of high and low BG.

However, the COVID-19 situation has created a challenging terrain for effective glycemic management (14). Amid pressures to flatten the pandemic curve, patients and clinicians may divert focus and resources away from diabetes management, resulting in compromised care (8). Moreover, home quarantine, physical distancing, and community containment—while enacted to ensure the safety of Americans—can erode chronic disease services and make it increasingly difficult for PWD to access medical supplies and engage in optimal self-management behaviour (e.g., healthy eating and physical

activity) (15). Previous outbreaks have also been associated with inadequate diabetes monitoring and barriers to accessing healthcare, medications, and testing supplies (4,8). Such disruptions to routine care can lead to worse glycemic outcomes during and after the event (16,17).

Yet, to date, most diabetes-related COVID-19 studies have focused exclusively on the epidemiology of hospitalized cases (18,19) and failed to consider how outpatient chronic diabetes management has suffered in the face of the pandemic. The lack of real-world evidence on the situational effects of COVID-19 bodes ill for the implementation of effective outbreak strategies that support Americans with diabetes. As the pandemic persists into the foreseeable future, the need to address this gap only intensifies.

The present investigation aims to chart the complex hinterland of COVID-19 as it intersects with America's other deadly pandemic: Diabetes. We measured how, and the extent to which, the COVID-19 situation has affected glycemic management in the general US population with type 1 and 2 diabetes. The results of this study will be instructive for handling chronic disease management both during the current public health emergency and in future.

RESEARCH DESIGN AND METHODS

Study design, participants, and data collection

We conducted a cross-sectional investigation of data collected from the real-world, population-based iNPHORM Study (Investigating Novel Predictions of Hypoglycemia Occurrence Using Real-world Models): an ambidirectional (one-year retrospective/one-year prospective) survey of outpatient Americans with diabetes.

iNPHORM participants were recruited from five pre-existing online panels of the general US public. Collectively, these panels comprised >10,000 Americans (≥18 years old) with type 1 diabetes and >58,000 with type 2 diabetes. Panel members 18-90 years old, living in the US for the past year, and with type 1 or 2 diabetes taking insulin and/or secretagogues were eligible to enroll in our study. Individuals were ineligible if they were or had been pregnant within the past year, were involved in an interventional study, or were unable to read/understand English.

Convenience sampling was used to enroll two waves of participants: Wave 1 and Wave 2. First, a randomly selected subset of the panels was targeted based on study requirements, mainly diabetes status. These individuals were contacted via email about

the study; those interested in participating were directed to complete a screening questionnaire. Recruitment of Wave 1 ended when we achieved our target sample size of 1250 eligible enrollees. Those in Wave 1 who failed to submit the Month 1 follow-up questionnaire were withdrawn from the study and replaced by new eligible recruits (Wave 2) sampled from a different, randomly selected subset of the panels. To finalize enrollment, Wave 1 and 2 eligible respondents needed to provide consent and complete the baseline questionnaire. Once enrolled, participants were managed and hosted by Ipsos Interactive Services (IIS).

Each recruitment wave, offset by two months, will complete up to 12 follow-up questionnaires disseminated on a prescheduled, monthly basis. Questionnaires must be submitted within seven-days of the distribution date. Reminders and honorariums are being administered to optimize participant retention.

Data collection will occur February-2020 to April-2021. Further details regarding the iNPHORM study, including sample size considerations, are available at clinicaltrials.gov (NCT04219514) (20).

Survey instruments and variables

All questionnaires (screening, baseline, and follow-ups) were developed by our team of epidemiologists and clinicians in consultation with the literature. Prior to dissemination, questionnaires were pretested via semi-structured interviews for content, comprehensibility, skip patterns, and length

In this study, we summarize data from 16 items contained in our COVID-19 sub-questionnaire (described below). This sub-questionnaire was added *post hoc* in response to the escalating severity of the US COVID-19 situation. Beginning with the 'Wave 1 second follow-up questionnaire (FQ2)' (administered April 21st-28th, 2020), each monthly follow-up will contain the COVID-19 sub-questionnaire. We herein analyze 'Wave 1-FQ2' data.

COVID-19 status: To ascertain self-reported infection status (past month), we adapted the CDC COVID-19 case definitions (April 2020) (21). Two structured items were developed to capture clinical criteria (symptoms), laboratory criteria (confirmed diagnoses), and epidemiologic linkage (potential exposure). Aligning with CDC recommendations, we classified respondents as confirmed, probable, or possible cases.

Confirmed cases were those who reported having been formally diagnosed with COVID-19. Probable cases were those who did not have a formal diagnosis but who reported 1) symptoms typical of COVID-19 *and* 2) ≥ 1 form of epidemiologic linkage. If only one of the two latter conditions was met, we classified individuals as possible cases.

Impact of the COVID-19 situation on aspects of diabetes management: We developed 12 structured, 5-point Likert items to assess how, and to what extent, the COVID-19 situation has disrupted socio-economic, behavioural/clinical, and psychosocial aspects of participants' diabetes management (past month). Respondents were asked to evaluate whether these aspects were made much harder, somewhat harder, somewhat easier, or much easier by the COVID-19 situation—a neutral option was provided. Topics included drug affordability/accessibility, medication-taking behaviour, healthcare consultations, glucose monitoring, and social support. Additionally, we incorporated two structured, binary items to assess drug rationing.

Socio-demographic and clinical characteristics of study sample: Self-reported socio-demographic and clinical characteristics were collected between the screening,

baseline, FQ1, and FQ2 questionnaires. Past-month frequencies of self-reported severe hypoglycemia (SH) and non-severe hypoglycemia (NSH), defined in accordance with the ADA (22), were assessed at FQ2. Non-severe hypoglycemia was defined as any event that could be self-treated; SH was defined as a medical emergency that could not be self-treated (e.g., required third-party assistance).

Statistical analysis

Categorical variables were summarized as frequencies and percentages, while continuous variables as means and standard deviations (SD) or medians and interquartile ranges (IQR). Crude hypoglycemia frequencies were calculated as incidence rates (IR) and incidence proportions (IP). Confirmed, probable, and possible COVID-19 cases were calculated as period prevalences.

The impact of the COVID-19 situation on glycemic management was descriptively analyzed (Likert responses were trichotomized). Differences by diabetes type were assessed using the Wilcoxin-Mann-Whitney test for Likert responses and the two-sample test of proportions for binary responses. Tests were two-sided at α=0.05. Analyses were performed using STATA V.16.0.

Patient and public involvement

No patients were directly involved in designing or conducting this study.

Ethical considerations

Western investigators and IIS obtained approval from the Western University's Research Ethics Board and the Pearl Institutional Review Board (US), respectively.

RESULTS

The current evaluation is based on a sub-sample of 667 (type 1 diabetes: 18.0%; type 2 diabetes: 82%) out of 704 Wave 1-FQ2 respondents who reported taking insulin and/or secretagogues (i.e., were at-risk of hypoglycemia). Socio-demographic and clinical characteristics are summarized in Table 1. Half of participants were female. The mean age was 51.9 (SD: 14.6; Min, Max: 20, 87) years; 23.2% were $\geq$ 65 years old. Diabetes duration was 26.0 (IQR: 23.0) years in people with type 1 and 11.0 (IQR: 14.0) years in people with type 2 diabetes.

All respondents with type 1 diabetes, and 38.4% with type 2 diabetes, reported taking insulin without secretagogues; among the remaining participants with type 2 diabetes, 36.9% were taking secretagogues without insulin, and 24.7% were taking a combination

of insulin and secretagogues. Twenty-three percent (type 1 diabetes: 23.3%; type 2 diabetes: 23.0%) of the total sample reported A1C values $\geq$ 8.1%. Sixty-one percent reported $\geq$ 1 diabetes-related complication, while 83.2% reported $\geq$ 1 comorbidity. Table 2 summarizes self-reported hypoglycemia incidences (combined daytime and nocturnal). The IR and IP of NSH were higher in people with type 1 diabetes (IR: 5.7 [95%CI: 4.6-7.1] events per person-month (PPM) and IP: 83.3% [95%CI: 75.7-88.9]) versus type 2 diabetes (IR: 2.1 [95%CI: 1.8-2.4] events PPM and IP: 55.0% [95%CI: 50.8-59.1]). However, SH, occurring at an overall rate of 0.7 (95%CI: 0.5-0.96) events PPM, was almost twice as common in people with type 2 versus type 1 diabetes (0.8 [95%CI: 0.5-1.1] versus 0.4 [95%CI: 0.2-0.9] events PPM]). Similarly, the monthly IP of SH, affecting nearly 13% (95%CI: 10.6-15.7) of respondents, was higher in people with type 2 diabetes compared to type 1 diabetes (13.2% [95%CI: 10.6-16.3] versus 11.7% [95%CI: 7.08-18.6]).

The one-month period prevalences of confirmed, probable, and possible COVID-19 were 0.75%, 0.75%, and 8.9%, respectively (Table 3).

The impact of the COVID-19 situation on aspects of glycemic management

A summary of results are provided in Table 4. Almost a quarter of respondents (type 1 diabetes: 30.0%; type 2 diabetes: 23.0%, *P*-value =0.07) reported that the COVID-19 situation had made affording rent and other living expenses somewhat or much harder. Similarly, 27.6% (type 1 diabetes: 23.3%; type 2 diabetes: 28.5%, *P*-value =0.29) of participants expressed difficulties ensuring adequate food supply to avoid hypoglycemia. Close to one in five experienced challenges paying for their diabetes medications (type 1 diabetes: 16.7%; type 2 diabetes: 19.0%, *P*-value =0.66) or test strips/sensors (type 1 diabetes: 13.3%; type 2 diabetes: 18.3%, *P*-value =0.31). Amid affordability concerns, access-related issues in retrieving diabetes medications from the pharmacy were noted by 27.4% (type 1 diabetes: 30.8%; type 2 diabetes: 26.7%, *P*-value =0.26) of our study sample. As well, because of the COVID-19 situation, ~17% of participants reported rationing their diabetes medications either to make supplies last longer (type 1 diabetes: 13.3%; type 2 diabetes: 17.4%, *P*-value =0.28) or avoid hypoglycemia (overall: 16.8%; type 1 diabetes: 15.8%; type 2 diabetes: 17.0%, *P*-value =0.76).

The COVID-19 situation also influenced participants' abilities to self-manage. Many respondents struggled to remember to take their diabetes medication(s) as prescribed (overall: 13.6%; type 1 diabetes: 6.7%; type 2 diabetes: 15.2%, *P*-value =0.052) as well as test and monitor their BG (overall: 15.9%; type 1 diabetes: 5.0%; type 2 diabetes: 18.3%, *P*-value <0.001) and risk of hypoglycemia regularly (overall: 12.0%; type 1 diabetes: 7.5%; type 2 diabetes: 13.0%, *P*-value =0.02). Over a third of respondents (type 1 diabetes: 35.0%; type 2 diabetes: 36.8%, *P*-value =0.78) found it somewhat or much harder to consult with their diabetes care providers. In terms of exercise maintenance, almost one in two respondents (type 1 diabetes: 47.5%; type 2 diabetes: 46.1, *P*-value =0.98) reported that it had been somewhat or much harder to stay as physically active as usual.

Lastly, psychosocial effects were observed. Many participants (14.5%) felt less in control of their hypoglycemia (type 1 diabetes: 11.7%; type 2 diabetes: 15.2%, *P*-value =0.5); 19% also reported having insufficient social support to help manage their risk (type 1 diabetes: 10.8%; type 2 diabetes: 20.3%, *P*-value =0.06).

The COVID-19 situation rarely had a beneficial impact on participants' lives. For almost all aspects of diabetes management that were measured, <5% of the sample selected "somewhat easier" or "much easier".

DISCUSSION

Experts have long been aware of the impacts a protracted emergency would have on healthcare and outcomes. Now, as two widespread pandemics collide, many Americans are finding themselves at the nidus of extreme clinical vulnerability, and with little support. Despite advice furnished by several national and international organizations, PWD are clearly struggling to maintain glycemic management standards during the pandemic. This gap forebodes important, population-based consequences to diabetes-related morbidities, both now and well-after vaccinations are distributed.

Our study is the first and most comprehensive investigation to quantify the impact of the COVID-19 situation on the socio-economic, behavioural/clinical, and psychosocial aspects of glycemic management in US outpatient communities. In general, the pandemic was found to cause substantial deficiencies in routine diabetes care. Of note,

only few appreciable differences were observed by diabetes type; of those identified, most related to the behavioural aspects of glycemic management.

COVID-19 and the socio-economic aspects of glycemic management

People with diabetes have been severely and disproportionately affected by the pandemic. Based on recent data published by the ADA, 24% of PWD have been forced to use savings, loans, or money from their stimulus checks (23). This percentage increases to half among the 33% of PWD (compared to 29% of people without diabetes) who have lost income since the pandemic began (23). It is thus not surprising that almost a quarter of iNPHORM respondents revealed that the COVID-19 situation impeded their abilities to afford rent and other living expenses. As the outbreak continues to escalate across the country, it is expected that the financial situation of many Americans will become increasingly precarious (18).

In this study, economic incertitude also affected participants' access to healthy food (9). COVID-19-related financial or environmental factors can invoke a state of food insecurity, a major predictor of clinically significant hypoglycemia (24). One US study found that exhaustion of food budgets was associated with a 27% increase in

hypoglycemia-related hospital admissions (25). Other research has associated food insecurity among PWD with poorer glucose monitoring and higher A1C values (26). Furthermore, decreases in financial resources, especially in the absence of health coverage, can inhibit access to diabetes medical supplies. An American study found that prescription refills for diabetes medications fell by 10% between January and August 2020 (27); however, whether or not this was due to financial or environmental factors was unclarified. Our data reveal that while roughly 20% of respondents experienced difficulties affording medications or strips/sensors, over a quarter reported issues physically retrieving medical supplies from pharmacies (perhaps due to prevention orders or anxieties over potential exposure).

Interruptions in healthcare access may explain the significant percentages of respondents who reported rationing their diabetes supplies. Our study investigated whether or not PWD ration their medications not just to extend their lifespan, but to prevent hypoglycemia. Despite evidence that lockdown exacerbates hypoglycemia risk (28), no research yet existed measuring the potential risk of hypoglycemia-specific medication rationing during COVID-19. Treatment rationing contradicts the CDC's

recommendations for managing diabetes during the pandemic (11). Not only can antihyperglycemic underuse increase the likelihood of deleterious short-term outcomes, but it can also drive up the cost of long-term diabetes-related complications (29). The impact of the COVID-19 situation on socio-economic indicators predictably did not vary by diabetes type with nearly equivalent percentages of each reporting financial and environmental instabilities because of the pandemic.

COVID-19 and the behavioural/clinical aspects of glycemic management

Evidence from past national emergencies underscores their profound and lasting implications on self-management behaviours in people with coexistent illnesses (16,17). Our study is the most comprehensive diabetes investigation to measure these implications in the COVID-19 era. Because of the pandemic, several iNPHORM participants reported forgetting to take their prescribed medications. This was especially true of type 2 diabetes respondents, perhaps due to variability in medication regimens compared to those with type 1 diabetes. Lapses in medication use can compromise therapeutic adherence and efficacies, leading to elevated A1C values as far-out as 16 months post-emergency (17). This risk is compounded by sub-optimal BG tracking.

Many respondents, especially those with type 2 diabetes, reported difficulties testing/monitoring their glucose and, specifically, hypoglycemia risk.

In addition, the pandemic has imposed dramatic changes on routine healthcare access and delivery, particularly among individuals with underlying health conditions (30). To prioritize access to hospital beds, equipment, and staff, as well as to minimize viral transmission, much of routine healthcare has been postponed or cancelled. As well, patients themselves may decline attendance at hospitals, clinics, and screening exams over concerns of infection. More than a third of respondents indicated that the COVID-19 situation made it harder to consult with their diabetes providers. Interestingly, this finding did not significantly differ by diabetes type.

Research has shown that deferred or avoided healthcare due to the pandemic can contribute to excess morbidity and mortality (31). Based on an article by Woolf SH et al. (32), US states with large numbers of COVID-19-related deaths experience large proportional increases in deaths from other underlying causes, including diabetes. Impacts on health may worsen the longer community containment measures last. A simulation study of data from previous global disasters found the duration of lockdown

to be directly proportional to A1C and number of diabetes-related complications (33). Unfortunately, these effects may endure even after the viral outbreak has been quelled. Evidence from past disasters, has shown that reduced access to healthcare during the acute phase of an emergency can lead to an aftermath of increased deaths and morbidities including stroke, myocardial infarctions, and diabetes-related complications (34).

Finally, COVID-19 mitigation measures can restrict access to indoor and outdoor physical activities, contributing to increased sedentary behaviours that adversely affect immune defence, glycemic control, and metabolic health in general (9). Based on data from other viral infections, sub-optimal physical activity can accentuate symptom severity, recovery times, and transmissibility; it can also compromise post-vaccination immunity and increase secondary infection risk (35). Regardless of diabetes type, staggering percentages of participants reported reduced physical activity because of the pandemic, a sure warning sign of the extensive health consequences to come.

COVID-19 and the psychosocial aspects of glycemic management

The psychosocial ramifications of COVID-19 in PWD has been minimally investigated in the literature. Our study specifically assessed how the pandemic has impacted respondents' senses of personal control over their hypoglycemia risk. Significant decrements in self-perceived control were observed across all participants. Sense of control—the learned belief that one does master, control, and shape one's life—has been linked to several positive health effects including proactive behavior and emotional well-being (36). However, inadequate supplies, financial loss, fear psychosis of being infected, and media/disinformation can all contribute to increased feelings of powerlessness (37). Reductions in sense of personal control have been associated with heightened stress, anxiety, and depressive symptoms (38)—outcomes that have been linked to poor medication adherence and diminished self-management (39).

While support from family and friends can mediate the contextual impacts of COVID-19, several respondents in our study, particularly those with type 2 diabetes, reported insufficient social support to help manage their hypoglycemia. Assistance from informal relationships has been identified as a major component to hypoglycemia self-management with demonstrable impacts on diabetes-related morbidity and mortality

reduction (14,38,40). The gap in social support observed in our study portend troubling implications for hypoglycemia incidence as well as other clinical and psychosocial sequelae. No study had yet quantified the effect the COVID-19 situation on social support access in PWD.

Study strengths and limitations

This study evaluates a large, generalized outpatient cohort of diabetic Americans—with and without infection—to derive insight into the real-world, real-time consequences of the COVID-19 situation in diabetes. The sample cohort focused on insulin and/or secretagogues users so variations in hypoglycemia management could be ascertained; such data had yet to be garnered in the US. By developing a novel pandemic-specific questionnaire, our research team was able to estimate the direct repercussions of the COVID-19 situation in Americans with diabetes.

However, certain limitations should be noted. First, though counteracted by the high national prevalence of internet users and rigorous sampling strategies, non-response and coverage bias may have influenced study results. Second, self-reported data may have been subject to information bias. To reduce this risk, measures were taken to

optimize recall intervals. Participants could also take time to reflect on items and/or review clinical documentation prior to completing the question/survey. Finally, estimates derived in our study may be conservative, as they stem from a one-month data capture in the early phase of the pandemic trajectory.

CONCLUSIONS

A 'hinterland' is defined as an area lying beyond what is visible or known. As a society we have exhibited unparalleled bravery in the face of one of the most terrifying crises known to humankind. However, our mission to abate the pandemic is only just beginning. Indeed, the COVID-19 calamity has had untold reverberations in the lives of Americans, extending well-beyond the visible devastations caused by infection alone. Not least are the impacts COVID-19 has had on PWD—cases and non-cases alike—who have struggled to maintain control of their disease amidst the pandemic. Yet, until now, the nature and scale of these impacts were largely unknown or uncharacterized. Thus, the results of our study draw not only awareness to the far-reaching and potential lasting consequences of the pandemic, but offer an evidence

base for decisive action. In identifying the unique needs of Americans with diabetes during the COVID-19 era, we can begin to develop, implement, and assess clinical and public health strategies that ensure safe, undisrupted care within the context of patients' communities. As we combat the acute phase of COVID-19, we must not lose sight of the pernicious health challenges that coexist and await us in the aftermath.

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Table 1. Socio-demographic and clinical characteristics of study sample

SOCIO-DEMOGRAPHIC CHARACTERISTICS		Total N=667	Type 1 Diabetes 120 (17.99%)	Type 2 Diabetes 547 (82.01%)
Age, mean (SD)				
	Years	51.85 (14.57)	45.96 (14.43)	53.14 (14.29)
Age (categorical), n (%)				
	≥ 18 and ≤ 40 years	180 (26.99)	51 (42.50)	129 (23.58)
	≥ 41 and ≤ 64 years	332 (49.78)	53 (44.17)	279 (51.01)
	≥ 65 and ≤ 74 years	123 (18.44)	11 (9.17)	112 (20.48)
	≥ 75 years	32 (4.80)	5 (4.17)	27 (4.94)
Sex assigned at birth, n (%)				
	Female	341 (51.12)	80 (66.67)	261 (47.71)
	Male	326 (48.88)	40 (33.33)	286 (52.29)
Race, n (%)				
	White	555 (83.21)	111 (92.50)	444 (81.17)
	Black or African American	52 (7.80)	3 (2.50)	49 (8.96)
	Asian	17 (2.55)	3 (2.50)	14 (2.56)

Hispanic, Latino/a, or Spanish origin	13 (1.95)	1 (0.83)	12 (2.19)
American Indian, Alaska Native, Native Hawaiian, or Pacific Islander	4 (0.60)	0	4 (0.73)
Multiracial	23 (3.45)	2 (1.67)	21 (3.84)
Other	3 (0.45)	0	3 (0.55)
Hispanic, Latino/a, or Spanish origin, n (%)			
Mexican, Mexican American, Chicano	27 (4.05)	2 (1.67)	25 (4.57)
Puerto Rican	6 (0.90)	1 (0.83)	5 (0.91)
Cuban	2 (0.30)	0	2 (0.37)
Other Hispanic, Latino/a, or Spanish origin	3 (0.45)	1 (0.83)	2 (0.37)
Not of Hispanic, Latino/a, or Spanish origin	629 (94.30)	116 (96.67)	513 (93.78)
Highest level of education at time of study enrolment, n (%)			
Elementary or high school (No diploma)	10 (1.50)	3 (2.50)	7 (1.28)
High school diploma or GED/alternative credential	101 (15.14)	19 (15.83)	82 (14.99)
College degree or some college	425 (63.72)	75 (62.50)	350 (63.99)
Degree beyond completing first college Bachelor's degree	131 (19.64)	23 (19.17)	108 (19.74)
Employment status at time of study enrolment, n (%)			
Employed full-time or part-time (including self-employment)	346 (51.87)	73 (60.83)	273 (49.91)
Temporarily laid off/Temporarily unemployed due to a health issue	4 (0.60)	1 (0.83)	3 (0.55)

Unable to work due to disability	84 (12.59)	11 (9.17)	73 (13.35)
Unemployed	55 (8.25)	15 (12.50)	40 (7.31)
Student	4 (0.60)	1 (0.83)	3 (0.55)
Retired	174 (26.09)	19 (15.83)	155 (28.34)
Total annual household income (before taxes and deductions) at time of study enrolment, n (%)*			
<$24,999	107 (16.21)	13 (11.21)	94 (17.28)
$25,000 to $54,999	173 (26.21)	25 (21.55)	148 (27.21)
$55,000 to $84,999	142 (21.52)	39 (33.62)	103 (18.93)
$85,000 to $114,999	109 (16.52)	22 (18.97)	87 (15.99)
≥ $115,000	129 (19.55)	17 (14.66)	112 (20.59)
Healthcare insurance at time of study enrolment, n (%)			
Insurance through a current or former employer or union that is not a high deductible plan†	153 (22.94)	36 (30.00)	117 (21.39)
Insurance purchased directly from insurance company that is not a high deductible plan	49 (7.35)	11 (9.17)	38 (6.95)
High deductible plan	34 (5.10)	11 (9.17)	23 (4.20)
Medicare	77 (11.54)	7 (5.83)	70 (12.80)
Medicaid, Medical Assistance, or other government-assistance plan	74 (11.09)	17 (14.17)	57 (10.42)
TRICARE and Veterans Affairs	9 (1.35)	2 (1.67)	7 (1.28)

Other	5 (0.75)	2 (1.67)	3 (0.55)
Two or more insurance plans	257 (38.53)	32 (26.67)	225 (41.13)
No insurance coverage at all	9 (1.35)	2 (1.67)	7 (1.28)

CLINICAL CHARACTERISTICS	Total N=667	Type 1 Diabetes 120 (17.99%)	Type 2 Diabetes 547 (82.01%)
Duration of diabetes, median (IQR)			
Years	13 (15)	26 (23)	11 (14)
Most recent hemoglobin A1C, n (%)*			
≤ 7% (53 mmol/mol)	252 (37.78)	45 (37.50)	207 (37.84)
7.1% (54 mmol/mol) to 8% (64 mmol/mol)	239 (35.83)	45 (37.50)	194 (35.47)
8.1% (65 mmol/mol) to 9% (75 mmol/mol)	99 (14.84)	14 (11.67)	85 (15.54)
≥ 9.1% (76 mmol/mol)	55 (8.25)	14 (11.67)	41 (7.50)
Unsure	12 (1.80)	0	12 (2.19)
Body mass index (BMI) at time of study enrolment, median (IQR)			
BMI (kg/m^2)	30.38 (11.87)	26.43 (6.18)	32.19 (11.99)
Current insulin and/or secretagogue use, n (%)			

Insulin *without* Secretagogues	330 (49.48)	120 (100.00)	210 (38.39)
Secretagogues *without* Insulin	202 (30.28)	0	202 (36.93)
Insulin *in combination with* Secretagogues	135 (20.24)	0	135 (24.68)
Diagnosed diabetes-related complications since 1 year preceding study enrolment, n (%)‡			
No complications	263 (39.43)	41 (34.17)	222 (40.59)
One or more complications	404 (60.57)	79 (65.83)	325 (59.41)
Amputation	91 (13.64)	12 (10.00)	79 (14.44)
Diabetes Ketoacidosis	110 (16.49)	42 (35.00)	68 (12.43)
Foot damage	123 (18.44)	18 (15.00)	105 (19.20)
Gastroparesis	95 (14.24)	20 (16.67)	75 (13.71)
Hyperosmolar hyperglycemic nonketotic coma	60 (9.00)	5 (4.17)	55 (10.05)
Nephropathy	114 (17.09)	18 (15.00)	96 (17.55)
Neuropathy	298 (44.68)	46 (38.33)	252 (46.07)
Retinopathy	156 (23.39)	46 (38.33)	110 (20.11)
Comorbidity status at time of study enrolment, n (%)‡			
No comorbidities	112 (16.79)	32 (26.67)	80 (14.63)
One or more comorbidities	555 (83.21)	88 (73.33)	467 (85.37)
Bone, joint, or muscle problem	310 (46.48)	39 (32.50)	271 (49.54)
Cancer	52 (7.80)	3 (2.50)	49 (8.96)

Cardiovascular condition	128 (19.19)	17 (14.17)	111 (20.29)
Chronic kidney disease	73 (10.94)	8 (6.67)	65 (11.88)
Chronic liver failure or liver disease	39 (5.85)	2 (1.67)	37 (6.76)
Eating disorder	35 (5.25)	7 (5.83)	28 (5.12)
Gastrointestinal disease	86 (12.89)	17 (14.17)	69 (12.61)
HIV/AIDS	11 (1.65)	2 (1.67)	9 (1.65)
Hypertension	363 (54.42)	50 (41.67)	313 (57.22)
Mental health condition	223 (33.43)	36 (30.00)	187 (34.19)
Neurological disorder	39 (5.85)	8 (6.67)	31 (5.67)
Physical impairment	168 (25.19)	29 (24.17)	139 (25.41)
Respiratory condition	125 (18.74)	24 (20.00)	101 (18.46)
Stroke or transient ischemic attack	44 (6.60)	5 (4.17)	39 (7.13)
Current continuous glucose monitoring device use, n (%)			
Yes	229 (34.33)	65 (54.17)	164 (29.98)

SD, standard deviation; IQR, interquartile range

* Cumulative percentage <100% due to missing data

† High Deductible Plan: Deductible >$1,350 for an individual or >$2,700 for a family

‡ Cumulative percentage >100% as participants could select more than one response

Table 2. Incidence rates and proportions of severe and non-severe hypoglycemia (daytime + nocturnal), overall and by diabetes type

INCIDENCE RATES	Total N=667	Type 1 Diabetes 120 (17.99%)	Type 2 Diabetes 547 (82.01%)
Severe Hypoglycemia			
Events per person-month (95% CI)	0.68 (0.48-0.96)	0.39 (0.18-0.85)	0.75 (0.51-1.09)
Non-Severe Hypoglycemia			
Events per person-month (95% CI)	2.75 (2.43-3.11)	5.73 (4.60-7.13)	2.10 (1.82-2.41)
INCIDENCE PROPORTIONS	**Total N=667**	**Type 1 Diabetes 120 (17.99%)**	**Type 2 Diabetes 547 (82.01%)**
Severe Hypoglycemia (past month)			
% with $\geq$ 1 event (95% CI)	12.91 (10.58-15.67)	11.67 (7.08-18.63)	13.19 (10.60-16.28)
Non-Severe Hypoglycemia (past month)			
% with $\geq$ 1 event (95% CI)	60.06 (56.29-63.71)	83.33 (75.66-88.94)	54.95 (50.75-59.07)

CI, confidence interval.

Table 3. Period prevalence of COVID-19 infection*

PERIOD PREVALENCE OF COVID-19	Total N=667	Type 1 Diabetes 120 (17.99%)	Type 2 Diabetes 547 (82.01%)
Confirmed (past month), n (%)†			
	5 (0.75)	0	5 (0.91)
Probable (past month), n (%)‡			
	5 (0.75)	0	5 (0.91)
Possible (past month), n (%)§			
	59 (8.86)	16 (13.33)	43 (7.86)

* Data collected April 21st-28th, 2020

† Had a formal diagnosis of COVID-19

‡ No formal diagnosis of COVID-19; reported 1) symptoms typical of COVID-19 *and* 2) at least one form of epidemiologic linkage

§ No formal diagnosis of COVID-19; reported 1) symptoms typical of COVID-19 *or* 2) at least one form of epidemiologic linkage

Table 4. Impact of the COVID-19 situation on aspects of participants' glycemic management (past month)*

ASPECT OF GLYCEMIC MANAGEMENT	...has been much/ somewhat harder...	...has not been impacted	... has been much/somewhat easier...	(R) *P*-value†
...Affording rent and other living expenses				
Overall (N=667)	162 (24.29)	491 (73.61)	14 (2.10)	0.07
Type 1 Diabetes (n=120)	36 (30.00)	83 (69.17)	1 (0.83)	
Type 2 Diabetes (n=547)	126 (23.03)	408 (74.59)	13 (2.38)	
...Ensuring enough food to avoid hypoglycemia				
Overall (N=667)	184 (27.59)	475 (71.21)	8 (1.20)	

Type 1 Diabetes (n=120)	28 (23.33)	91 (75.83)	1 (0.83)	0.29
Type 2 Diabetes (n=547)	156 (28.52)	384 (70.20)	7 (1.28)	
...Affording diabetes medication(s)				
Overall (N=667)	124 (18.59)	534 (80.06)	9 (1.35)	0.66
Type 1 Diabetes (n=120)	20 (16.67)	99 (82.50)	1 (0.83)	
Type 2 Diabetes (n=547)	104 (19.01)	435 (79.52)	8 (1.46)	
...Affording test strips and/or sensors				
Overall (N=667)	116 (17.39)	540 (80.96)	11 (1.65)	0.31
Type 1 Diabetes (n=120)	16 (13.33)	103 (85.83)	1 (0.83)	
Type 2 Diabetes (n=547)	100 (18.28)	437 (79.89)	10 (1.83)	
...Retrieving diabetes medication(s) from the pharmacy				
Overall (N=667)	183 (27.44)	470 (70.46)	14 (2.10)	0.26
Type 1 Diabetes (n=120)	37 (30.83)	82 (68.33)	1 (0.83)	
Type 2 Diabetes (n=547)	146 (26.69)	388 (70.93)	13 (2.38)	
...Consulting with healthcare provider(s) about diabetes				
Overall (N=667)	243 (36.43)	410 (61.47)	14 (2.10)	0.78
Type 1 Diabetes (n=120)	42 (35.00)	76 (63.33)	2 (1.67)	
Type 2 Diabetes (n=547)	201 (36.75)	334 (61.06)	12 (2.19)	
...Testing/monitoring blood glucose				
Overall (N=667)	106 (15.89)	551 (82.61)	10 (1.50)	<0.001‡
Type 1 Diabetes (n=120)	6 (5.00)	110 (91.67)	4 (3.33)	
Type 2 Diabetes (n=547)	100 (18.28)	441 (80.62)	6 (1.10)	

...Remembering to take diabetes medication(s) as prescribed				
Overall (N=667)	91 (13.64)	554 (83.06)	22 (3.30)	
Type 1 Diabetes (n=120)	8 (6.67)	109 (90.83)	3 (2.50)	0.052
Type 2 Diabetes (n=547)	83 (15.17)	445 (81.35)	19 (3.47)	
...Monitoring risk of hypoglycemia regularly				
Overall (N=667)	80 (11.99)	561 (84.11)	26 (3.90)	
Type 1 Diabetes (n=120)	9 (7.50)	103 (85.83)	8 (6.67)	0.02‡
Type 2 Diabetes (n=547)	71 (12.98)	458 (83.73)	18 (3.29)	
...Staying as physically active as usual				
Overall (N=667)	309 (46.33)	329 (49.33)	29 (4.35)	
Type 1 Diabetes (n=120)	57 (47.50)	55 (45.83)	8 (6.67)	0.98
Type 2 Diabetes (n=547)	252 (46.07)	274 (50.09)	21 (3.84)	
...Feeling in control of hypoglycemia				
Overall (N=667)	97 (14.54)	528 (79.16)	42 (6.30)	
Type 1 Diabetes (n=120)	14 (11.67)	99 (82.50)	7 (5.83)	0.50
Type 2 Diabetes (n=547)	83 (15.17)	429 (78.43)	35 (6.40)	
...Having enough social support to help manage hypoglycemia				
Overall (N=667)	124 (18.59)	518 (77.66)	25 (3.75)	
Type 1 Diabetes (n=120)	13 (10.83)	104 (86.67)	3 (2.50)	0.06
Type 2 Diabetes (n=547)	111 (20.29)	414 (75.69)	22 (4.02)	

ASPECT OF GLYCEMIC MANAGEMENT	Yes	No	*P*-value§
...Rationing diabetes medication(s) to make supplies last longer			
Overall (N=667)	111 (16.64)	556 (83.36)	
Type 1 Diabetes (n=120)	16 (13.33)	104 (86.67)	0.28
Type 2 Diabetes (n=547)	95 (17.37)	452 (82.63)	
...Rationing diabetes medication(s) to avoid hypoglycemia			
Overall (N=667)	112 (16.79)	555 (83.21)	
Type 1 Diabetes (n=120)	19 (15.83)	101 (84.17)	0.76
Type 2 Diabetes (n=547)	93 (17.00)	454 (17.00)	

n (%) are presented.

* Data collected April 21st-28th, 2020

† Item responses were compared between individuals with type 1 diabetes and type 2 diabetes. *P*-values were computed using two-sample Wilcoxin-Mann-Whitney tests.

‡ Statistically significant at an alpha value of 0.05 (i.e., the underlying distributions of item responses statistically significantly differed by diabetes type).

§ Item responses were compared between individuals with type 1 diabetes and type 2 diabetes. *P*-values were computed using two-sample Z tests for proportions.

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The COVID-19 Hinterland: Surveilling the self-reported impacts of the pandemic on diabetes management in the United States (Cross-sectional results of the iNPHORM Study)

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ABSTRACT

Main Objective: To determine how and to what extent, COVID-19 has affected real-world, self-reported glycemic management in Americans with type 1 or type 2 diabetes taking insulin and/or secretagogues, with or without infection.

Design: A cross-sectional sub-study using data from the iNPHORM panel survey.

Settings: United States (US).

Participants: Americans 18 to 90 years old with type 1 or 2 diabetes taking insulin and/or secretagogues were conveniently sampled from a probability-based internet panel.

Primary Outcome Measure: A structured, COVID-19-specific questionnaire was administered to assess the impact of the pandemic (irrespective of infection) on socio-economic, behavioural/clinical, and psychosocial aspects of glycemic management.

Results: Data from 667 respondents (type 1 diabetes: 18%; type 2 diabetes: 82%) were analyzed. Almost 25% reported A1C values ≥8.1%. Rates of severe and non-severe hypoglycemia were 0.68 (95%CI: 0.5 to 0.96) and 2.75 (95%CI: 2.4 to 3.1) events per-person month, respectively. Ten respondents reported a confirmed or probable COVID-19 diagnosis. Because of the pandemic, 24% of respondents experienced difficulties affording housing; 28% struggled to maintain sufficient food to avoid hypoglycemia; and 19% and 17% reported challenges accessing

diabetes therapies and testing strips, respectively. Over one-quarter reported issues retrieving antihyperglycemics from the pharmacy and over one-third reported challenges consulting with diabetes providers. The pandemic contributed to therapeutic non-adherence (14%), drug rationing (17%), and reduced monitoring (16%). Many struggled to keep track, and in control, of hypoglycemia (12 to 15%) and lacked social support to help manage their risk (19%). Nearly half reported decreased physical activity. Few statistically significant differences were observed by diabetes type.

Conclusions: COVID-19 was found to cause substantial self-reported deficiencies in glycemic management. Study results signal the need for decisive action to re-stabilize routine diabetes care in the US.

Trial registration: ClinicalTrials.gov Identifier: NCT04219514.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- This is the first US-based, primary research study to quantify the real-world, self-reported impact of the COVID-19 situation on the socio-economic, behavioural/clinical, and psychosocial aspects of glycemic management.

- A novel COVID-19-specific questionnaire was developed and administered to a real-world cohort of Americans with type 1 and type 2 diabetes taking insulin and/or secretagogues; study participants were recruited from a large, probability-based internet panel.
- Estimates presented in this study may be conservative as they describe the early phase of the pandemic.

SIGNIFICANCE OF THIS STUDY:

1. *What is already known about this subject?*

- The majority of COVID-19-related studies in the US have focused on hospitalized case epidemiology.
- Little is known about the peripheral impacts of the COVID-19 situation on glycemic management in Americans with diabetes taking insulin and/or secretagogues.
- Disruptions to services, resources, and self-management forebode important population-based consequences to diabetes-related morbidities, especially in the US where COVID-19 and diabetes eminently collide.

2. What this study adds

- The pandemic situation was found to cause substantial and diverse repercussions on participants' glycemic management, irrespective of diabetes type.
- The results of this study provide an instructive evidence base for improved diabetes care in the US, both during the current public health emergency and in future.

COVID-19 is among the most devastating health crises in global history. In the United States (US), the first reported infection occurred on January 19th, 2020.(1) Since then, the number of confirmed US-cases has surpassed 33.5 million, including over 605,000 deaths (July 5, 2021).(2)

People with diabetes (PWD) have been identified as clinically vulnerable to COVID-19. In the US, diabetes ranks as the second most common underlying health condition among all cases and has been connected to more severe infection.(3,4) However, less appreciated in the literature are the disruptions caused by the pandemic on routine diabetes care. These disruptions expose not only those with COVID-19, but all 34+ million Americans with diabetes to poor outcomes. Understanding how the pandemic affects diabetes services and management is crucial to informing short- and long-term clinical decision-making and public health planning. Targeted measures to help protect these Americans from the direct and indirect effects of the COVID-19 pandemic should be a top priority for all healthcare and government officials.

The complex hinterland of COVID-19 and diabetes

The pathophysiological benefits of glycemic control on diabetes outcomes have been well-established. Numerous studies have linked chronic hyperglycemia and glycemic variability to increased risks of micro- and macro-vascular complications and mortality. In addition, dysglycemia can potentiate immunosuppression,(5) increasing viral susceptibility and risk of poor clinical outcomes.(6) While the role of coexistent diabetes in the pathogenesis of COVID-19 is still being determined,(7) emerging signals suggest that euglycemia protects against infection and severity of prognoses.(8,9) These data are consistent with evidence from other viral infections where glucose control showed to augment host immune response.(5,10)

To mitigate COVID-19 risks, several national and international organizations have published diabetes pandemic guides, urging PWD to maintain scrupulous adherence to all self-management and public health recommendations.(7,8) Notably, the Centers for Disease Control and Prevention (CDC)(11) has recommended maintaining at least a 30-day supply of medication and 2-week supply of food. The American Diabetes Association (ADA)(12) has advised storing blood glucose emergency supplies (i.e., glucagon and ketone strips). And the International

Diabetes Federation(13) has encouraged healthy nutrition and regular monitoring to help avoid the complications of high and low blood glucose.

However, the COVID-19 situation has created a challenging terrain for effective glycemic management.(14) Amid pressures to flatten the pandemic curve, people with diabetes and their clinicians may divert focus and resources away from diabetes management, resulting in compromised care.(8) Moreover, home quarantine, physical distancing, and community containment—while enacted to ensure the safety of Americans—can erode chronic disease services and make it increasingly difficult for PWD to access medical supplies and engage in optimal self-management behaviour (e.g., healthy eating and physical activity).(15) Previous outbreaks have also been associated with inadequate diabetes monitoring and barriers to accessing healthcare, medications, and testing supplies.(4,8) Such disruptions to routine care can lead to worse glycemic outcomes during and after the event.(16,17)

Yet, to date, most diabetes-related COVID-19 studies in the US have focused exclusively on the epidemiology of hospitalized cases(18,19) and failed to consider how community-based chronic diabetes management has suffered in the face of the pandemic. The lack of real-world evidence on the situational effects of COVID-19 bodes ill for the implementation of effective

outbreak strategies that support Americans with diabetes. As the pandemic persists into the foreseeable future, the need to address this gap only intensifies.

The main objective of this investigation was to measure how, and the extent to which, the COVID-19 situation has affected self-reported glycemic management in the general community population of Americans with type 1 and 2 diabetes. In so doing, we aimed to chart the complex hinterland of COVID-19 as it intersects with America's other deadly epidemic: Diabetes. The results of this study will be instructive for handling chronic disease management both during the current public health emergency and in future.

RESEARCH DESIGN AND METHODS

Study design

This cross-sectional study describes the results of a COVID-19-specific sub-questionnaire that was administered as part of the larger iNPHORM (Investigating Novel Predictions of

Hypoglycemia Occurrence Using Real-world Models) panel survey: a one-year prospective analysis of real-world hypoglycemia risk stratification in the US (NCT04219514).(20)

Participants and data collection

iNPHORM participants were conveniently sampled from randomly selected subsets of a probability-based internet panel comprising >10,000 Americans with type 1 diabetes and >58,000 with type 2 diabetes (≥18 years old). These subsets were defined based on study requirements, mainly diabetes status. Individuals in each subset were contacted via email about the study; those interested in participating were directed to complete a screening questionnaire.

Panel members 18-90 years old, living in the US for the past year, and with type 1 or 2 diabetes taking insulin and/or secretagogues were eligible to enroll. Individuals were ineligible if they were or had been pregnant within the past year, were involved in an interventional study, or were unable to read/understand English. To finalize enrollment, eligible respondents needed to provide consent and complete a baseline questionnaire. Once enrolled, participants were

managed and hosted by Ipsos Interactive Services (IIS, www.ipsos.com), a leading global firm in diabetes insights and real-world survey conduct.

Respondent data were collected via the online IIS platform. In addition to the screener and baseline surveys, iNPHORM participants were asked to complete 12 prescheduled, monthly follow-up questionnaires. Follow-ups were required to be submitted within seven-days of the distribution date. Automatic reminders and notifications containing survey links were emailed throughout the prospective phase. As well, honoraria were issued in the form of e-gift cards; the incentivization scheme (based on the quantity and timing of completed surveys) complied with social standards of reciprocity and Western University's Research Ethics Board.

Owing to the escalating severity of COVID-19 in the US, iNPHORM follow-up questionnaires were emended post study commencement (at follow-up Month 2) to include a COVID-19-specific sub-questionnaire. The sub-questionnaire assessed community infection, and the impact of the pandemic on diabetes management. Data pertaining to the first administered COVID-19 sub-questionnaire (April 21st to 28th, 2020) are summarized herein.

Survey instruments and variables

iNPHORM questionnaires (screening, baseline, and follow-ups [including the COVID-19 sub-questionnaire]) were developed by our team of epidemiologists and clinicians in consultation with the literature. All surveys were designed to be completed in English on diverse internet-equipped devices (e.g., computers, smart phones, tablets). Efforts were taken to avoid double-barreled questions, clinical jargon, and value-laden or complex/ambiguous language. Additionally, each item was specified to ensure its mutual exclusivity, exhaustiveness, and appropriateness of detail. When necessary, concise, clearly worded preambles, instructions, and definitions (including expounding mouseover texts) were provided. Participants could take as much time as needed to reflect on items and/or review clinical documentation prior to completing the question/survey; at any point, they could opt out of responding. Questionnaires were piloted via semi-structured interviews prior to fielding.

COVID-19 status: To ascertain self-reported one-month infection status (March to April, 2020), we adapted the CDC COVID-19 case definitions (April 2020).(21) Two structured items were developed to capture clinical criteria (symptoms), laboratory criteria (confirmed diagnoses), and

epidemiologic exposure (e.g., close contact with a confirmed or suspected case; international travel). Aligning with CDC recommendations, we classified respondents as confirmed, probable, or possible cases. Confirmed cases were those who reported having been formally diagnosed with COVID-19. Probable cases were those who did not have a formal diagnosis but who reported 1) symptoms typical of COVID-19 *and* 2) ≥ 1 form of epidemiologic exposure. If only one of the two latter conditions was met, we classified individuals as possible cases.

Impact of the COVID-19 situation on aspects of diabetes management: We developed 12 structured, 5-point Likert items to assess how, on a scale from "much harder" to "much easier", "...the Coronavirus (COVID-19) situation has impacted..." various socio-economic, behavioural/clinical, and psychosocial aspects of participants' diabetes management (past month). A neutral option (the pandemic has had no impact) was ordered in the middle between negative and positive response categories. Topics included drug affordability/accessibility, medication-taking behaviour, healthcare consultations, glucose monitoring, and social support. Additionally, we incorporated two structured, binary items to assess drug rationing. See Appendix A for a complete list of these questions.

Socio-demographic and clinical characteristics of study sample: So as to align with the first administered COVID-19 sub-questionnaire (analyzed herein), socio-demographic and clinical characteristics were collated between the screening, baseline, and follow-up questionnaires Months 1 and 2. Past-month frequencies of self-reported severe hypoglycemia (SH) and non-severe hypoglycemia (NSH), defined in accordance with the ADA,(22) were assessed at follow-up Month 2. Non-severe hypoglycemia was defined as any event that could be self-treated; SH was defined as a medical emergency that could not be self-treated (e.g., required third-party assistance).

Statistical analysis

Categorical variables were summarized as frequencies and percentages, while continuous variables as means and standard deviations (SD) or medians and interquartile ranges (IQR). Crude hypoglycemia frequencies were calculated as incidence rates and proportions. Confirmed, probable, and possible COVID-19 cases were calculated as one-month period prevalences.

The impact of the COVID-19 situation on glycemic management was descriptively analyzed. Glycemic management was operationalized according to different important aspects from drug affordability/accessibility to social support. Variability by diabetes type was assessed using the Wilcoxin-Mann-Whitney test for Likert responses and the two-sample test of proportions for binary responses. Tests were two-sided at α=0.05. All estimates were based on complete case analyses and were computed using STATA V.16.0.

Patient and public involvement

Neither patients nor the public were directly involved in designing or conducting this study.

Ethical considerations

Western investigators and IIS obtained ethics approval from the Western University's Research Ethics Board and the Pearl Institutional Review Board (US), respectively (ID: 112986). Participants gave informed consent before taking part in the study.

RESULTS

A total of 704 iNPHORM participants completed the first COVID-19 sub-questionnaire (April, 2020). Of these respondents, 667 (type 1 diabetes: 18.0%; type 2 diabetes: 82%) reported taking insulin and/or secretagogues (i.e., met our study's eligibility criteria); their socio-demographic and clinical characteristics are summarized in Tables 1 and 2, respectively.

Of the 667 eligible respondents, half were female. The mean age was 51.9 (SD: 14.6; Min, Max: 20, 87) years with 23.2% ≥ 65 years old. Diabetes duration was 26.0 (IQR: 23.0) years in people with type 1 and 11.0 (IQR: 14.0) years in people with type 2 diabetes. All respondents with type 1 diabetes, and 38.4% with type 2 diabetes, reported taking insulin without secretagogues; among the remaining participants with type 2 diabetes, 36.9% were taking secretagogues without insulin, and 24.7% were taking a combination of insulin and secretagogues. Twenty-three percent (type 1 diabetes: 23.3%; type 2 diabetes: 23.0%) of the total sample reported A1C values ≥ 8.1%. Sixty-one percent reported ≥ 1 diabetes-related complication(s), while 83.2% reported ≥ 1 comorbidity.

Table 3 summarizes self-reported hypoglycemia incidences (combined daytime and nocturnal). The incidence rate and incidence proportion of NSH were higher in people with type 1 diabetes (incidence rate: 5.7 [95%CI: 4.6 to 7.1] events per person-month (PPM) and incidence proportion: 83.3% [95%CI: 75.7 to 88.9]) versus type 2 diabetes (incidence rate: 2.1 [95%CI: 1.8 to 2.4] events PPM and incidence proportion: 55.0% [95%CI: 50.8 to 59.1]). However, SH, occurring at an overall rate of 0.7 (95%CI: 0.5 to 0.96) events PPM, was almost twice as common in people with type 2 versus type 1 diabetes (0.8 [95%CI: 0.5 to 1.1] versus 0.4 [95%CI: 0.2 to 0.9] events PPM]). Similarly, the monthly incidence proportion of SH, affecting nearly 13% (95%CI: 10.6 to 15.7) of respondents, was higher in people with type 2 diabetes compared to type 1 diabetes (13.2% [95%CI: 10.6 to 16.3] versus 11.7% [95%CI: 7.08 to 18.6]).

The one-month period prevalences of confirmed, probable, and possible COVID-19 were 0.75% (T1DM: n=0; T2DM: n=5 [0.75%]), 0.75% (T1DM: n=0; T2DM: n=5 [0.75%]), and 8.9% (T1DM: n=16 [13.33%]; T2DM: n=43 [7.86%]), respectively.

The impact of the COVID-19 situation on aspects of glycemic management

A summary of results is provided in Tables 4 and 5. Almost a quarter of respondents (type 1 diabetes: 30.0%; type 2 diabetes: 23.0%, *P*-value =0.08) reported that the COVID-19 situation made affording rent and other living expenses either "somewhat harder" (type 1 diabetes: 19.2%; type 2 diabetes: 14.6%) or "much harder" (type 1 diabetes: 10.8%; type 2 diabetes: 8.4%). Similarly, 27.6% (type 1 diabetes: 16.7%; type 2 diabetes: 28.5%, *P*-value =0.29) of participants expressed it was "somewhat harder" (type 1 diabetes: 16.7%; type 2 diabetes: 20.1%) or "much harder" (type 1 diabetes: 6.7%; type 2 diabetes: 8.4%) to ensure adequate food supply to avoid hypoglycemia. Close to one in five experienced challenges paying for their diabetes medications (type 1 diabetes: 16.7%; type 2 diabetes: 19.0%, *P*-value =0.71) or test strips/sensors (type 1 diabetes: 13.3%; type 2 diabetes: 18.3%, *P*-value =0.38); of these individuals, approximately half reported that their ability to afford therapeutic supplies had been made "much harder" by the pandemic. Access-related issues were also identified. Overall, 27.4% (type 1 diabetes: 30.8%; type 2 diabetes: 26.7%, *P*-value =0.24) found the pandemic made it "somewhat harder" (overall: 18.7%; type 1 diabetes: 20.0%; type 2 diabetes: 18.5%) or "much harder" (overall: 8.7%; type 1 diabetes: 10.8%; type 2 diabetes: 8.2%) to retrieve diabetes medications from the pharmacy. As well, because of the COVID-19 situation, ~17% of participants reported rationing their diabetes

medications either to make supplies last longer (type 1 diabetes: 13.3%; type 2 diabetes: 17.4%, *P*-value =0.28) or avoid hypoglycemia (overall: 16.8%; type 1 diabetes: 15.8%; type 2 diabetes: 17.0%, *P*-value =0.76).

The COVID-19 situation also influenced participants' abilities to self-manage. Many respondents struggled to remember to take their diabetes medication(s) as prescribed (overall: 13.7%; type 1 diabetes: 6.7%; type 2 diabetes: 15.2%, *P*-value =0.047) as well as test and monitor their blood glucose (overall: 15.9%; type 1 diabetes: 5.0%; type 2 diabetes: 18.3%, *P*-value <0.001) and risk of hypoglycemia regularly (overall: 12.0%; type 1 diabetes: 7.5%; type 2 diabetes: 13.0%, *P*-value =0.026). Over a third of respondents (type 1 diabetes: 35.0%; type 2 diabetes: 36.8%, *P*-value =0.75) found it "somewhat harder" (overall: 23.7%; type 1 diabetes: 23.3%; type 2 diabetes: 23.8%) or "much harder" (overall: 12.7%; type 1 diabetes: 11.7%; type 2 diabetes: 13.0%) to consult with their diabetes care providers. In terms of exercise maintenance, almost one in two respondents (type 1 diabetes: 47.5%; type 2 diabetes: 46.1, *P*-value =0.84) reported that it had been "somewhat harder" (overall: 31.3%; type 1 diabetes: 30.0%; type 2 diabetes: 31.6%) or "much harder" (overall: 15.0%; type 1 diabetes: 17.5%; type 2 diabetes: 14.4%) to stay as physically active as usual.

Lastly, psychosocial effects were observed. Many participants (overall: 14.6%; type 1 diabetes: 11.7%; type 2 diabetes: 15.2%, *P*-value =0.5) felt the pandemic situation had made it "somewhat harder" (overall: 9.3%; type 1 diabetes: 7.5%; type 2 diabetes: 9.7%) or "much harder" (overall: 5.3%; type 1 diabetes: 4.2%; type 2 diabetes: 5.5%) to remain in control of their hypoglycemia. Nineteen percent also reported having insufficient social support to help manage their risk (type 1 diabetes: 10.8%; type 2 diabetes: 20.3%, *P*-value =0.056); for 12.4% (type 1 diabetes: 8.3%; type 2 diabetes: 13.4%) accessing social support was "somewhat harder", while for 6.2% (type 1 diabetes: 2.5%; type 2 diabetes: 7.0%) it was "much harder".

Although approximately 50% of respondents believed the pandemic situation had no impact on their glycemic management, rarely was a beneficial impact on participants' lives observed. In general, less than 5% of the sample reported that the pandemic made aspects of their diabetes management either "somewhat easier" or "much easier".

DISCUSSION

Experts have long been aware of the impacts a protracted emergency would have on healthcare and outcomes. Now, as two life-altering diseases collide, many Americans are finding themselves at the nidus of extreme clinical vulnerability, and with little support. Despite advice furnished by several national and international organizations, PWD are clearly struggling to maintain glycemic management standards during the pandemic. This gap forebodes important, population-based consequences to diabetes-related morbidities, both now and well-after vaccinations are distributed.

iNPHORM is the first investigation to quantify the impact of the COVID-19 situation on the socio-economic, behavioural/clinical, and psychosocial aspects of glycemic management among community-dwelling Americans. Based on the results of our study, the pandemic was found to cause substantial deficiencies in routine diabetes care in the US, a finding consistent with international data published by the World Health Organization.(23) Of note, only few appreciable differences were observed by diabetes type; of those identified, most related to the behavioural aspects of glycemic management.

COVID-19 and the socio-economic aspects of glycemic management

People with diabetes have been severely and disproportionately affected by the pandemic. Based on recent data published by the ADA, 24% of PWD have been forced to use savings, loans, or money from their stimulus checks.(24) This percentage increases to half among the 33% of PWD (compared to 29% of people without diabetes) who have lost income since the pandemic began.(24) It is thus not surprising that almost a quarter of iNPHORM respondents revealed that the COVID-19 situation impeded their abilities to afford rent and other living expenses. As the outbreak continues to escalate across the country, it is expected that the financial situation of many Americans will become increasingly precarious.(18)

In this study, economic incertitude also affected participants' access to healthy food.(9) COVID-19-related financial or environmental factors can invoke a state of food insecurity, a major predictor of clinically significant hypoglycemia.(25) One US study found that exhaustion of food budgets was associated with a 27% increase in hypoglycemia-related hospital admissions.(26) Food insecurity among PWD has also been associated with poorer glucose monitoring and higher A1C values.(26)

Furthermore, decreases in financial resources, especially in the absence of health coverage, can inhibit access to diabetes medical supplies. An American study found that prescription refills for diabetes medications fell by 10% between January and August 2020(27); however, whether or not this was due to financial or environmental factors was unclarified. Our data reveal that while roughly 20% of respondents experienced difficulties affording medications or strips/sensors, over a quarter reported issues physically retrieving medical supplies from pharmacies (perhaps due to prevention orders or anxieties over potential exposure).

Interruptions in healthcare access may explain the significant percentages of respondents who reported rationing their diabetes supplies. Our study investigated whether or not PWD ration their medications not just to extend their lifespan, but to prevent hypoglycemia. Despite evidence that lockdown exacerbates hypoglycemia risk,(28) no research yet existed measuring the potential risk of hypoglycemia-specific medication rationing during COVID-19. Treatment rationing contradicts the CDC's recommendations for managing diabetes during the pandemic.(11) Not only can antihyperglycemic underuse increase the likelihood of deleterious short-term outcomes, but it can also drive up the cost of long-term diabetes-related complications.(29)

The impact of the COVID-19 situation on socio-economic indicators predictably did not vary by diabetes type with nearly equivalent percentages of each reporting financial and environmental instabilities because of the pandemic.

COVID-19 and the behavioural/clinical aspects of glycemic management

Evidence from past national emergencies underscores their profound and lasting implications on self-management behaviours in people with coexistent illnesses.(16,17) Our study is the first American diabetes investigation to measure these implications in the COVID-19 era. Because of the pandemic, several iNPHORM participants reported forgetting to take their prescribed medications. This was especially true of type 2 diabetes respondents, perhaps due to variability in medication regimens compared to those with type 1 diabetes. Lapses in medication use can compromise therapeutic adherence and efficacies, leading to elevated A1C values as far-out as 16 months post-emergency.(17) This risk is likely compounded by financial- and access-related issues resulting from the pandemic (described in previous section) as well as sub-optimal blood

glucose tracking. Many respondents, especially those with type 2 diabetes, reported difficulties testing/monitoring their glucose and, specifically, hypoglycemia risk.

In addition, the pandemic has imposed dramatic changes on routine healthcare access and delivery, particularly among individuals with underlying health conditions.(30) To prioritize access to hospital beds, equipment, and staff, as well as to minimize viral transmission, much of routine healthcare has been postponed or cancelled. As well, people with diabetes may decline attendance at hospitals, clinics, and screening exams over concerns of infection. More than a third of respondents indicated that the COVID-19 situation made it harder to consult with their diabetes providers. Interestingly, this finding did not significantly differ by diabetes type.

Research has shown that deferred or avoided healthcare due to the pandemic can contribute to excess morbidity and mortality.(31) Based on an article by Woolf SH et al.,(32) US states with large numbers of COVID-19-related deaths experience large proportional increases in deaths from other underlying causes, including diabetes. Impacts on health may worsen the longer community containment measures last. A simulation study of data from previous global disasters found the duration of lockdown to be directly proportional to A1C and number of diabetes-related complications.(33) Unfortunately, these effects may endure even after the viral outbreak

has been quelled. Evidence from past disasters, has shown that reduced access to healthcare during the acute phase of an emergency can lead to an aftermath of increased deaths and morbidities including stroke, myocardial infarctions, and diabetes-related complications.(34) Such increases in morbidity and mortality resulting from delayed and reduced healthcare access are especially concerning among iNPHORM participants, of whom almost 90% reported some comorbidity or diabetes-related complication.

Finally, COVID-19 mitigation measures can restrict access to indoor and outdoor physical activities, contributing to increased sedentary behaviours that adversely affect immune defence, glycemic control, and metabolic health in general.(9) Based on data from other viral infections, sub-optimal physical activity can accentuate symptom severity, recovery times, and transmissibility; it can also compromise post-vaccination immunity and increase secondary infection risk.(35) Regardless of diabetes type, staggering percentages of participants reported reduced physical activity because of the pandemic, a sure warning sign of the extensive health consequences to come.

COVID-19 and the psychosocial aspects of glycemic management

The psychosocial ramifications of COVID-19 in PWD have been minimally investigated in the literature. Our study specifically assessed how the pandemic has impacted respondents' senses of personal control over their hypoglycemia risk. Significant decrements in self-perceived control were observed across all participants. Sense of control—the learned belief that one does master, control, and shape one's life—has been linked to several positive health effects including proactive behavior and emotional well-being.(36) However, inadequate supplies, financial loss, fear psychosis of being infected, and media/disinformation can all contribute to increased feelings of powerlessness.(37) Reductions in sense of personal control have been associated with heightened stress, anxiety, and depressive symptoms(38)—outcomes that have been linked to poor medication adherence and diminished self-management.(39)

No study had yet quantified the effect the COVID-19 situation on social support access in PWD. While support from family and friends can mediate the contextual impacts of COVID-19, several respondents in our study, particularly those with type 2 diabetes, reported insufficient social support to help manage their hypoglycemia. Assistance from informal relationships has

been identified as a major component to hypoglycemia self-management with demonstrable impacts on diabetes-related morbidity and mortality reduction.(14,38,40) The gap in social support observed in our study portend troubling implications for hypoglycemia incidence as well as other clinical and psychosocial sequelae.

Indeed, sub-optimal social support among people with type 2 diabetes, compounded by inadequate hypoglycemia risk monitoring, could explain why SH was found to be more common in our respondents with type 2 versus type 1 diabetes. Though comparable overall hypoglycemia incidences have been observed in other real-world studies,(41) the 2018 InHypo-DM study(42) reported similarly higher SH events rates in people with type 2 versus type 1 diabetes. This finding suggests that important deficiencies—irrespective of the pandemic situation—may exist with regard to hypoglycemia education, management behaviors, and/or primary care in people with type 2 diabetes when compared to their type 1 diabetes counterpart. Parenthetically, unlike many other real-world hypoglycemia investigations that focus exclusively on insulin-treated diabetes,(43–45) it should be noted that 25% and 18% of participants in iNPHORM and InHypo-DM, respectively, reported taking insulin in combination with secretagogues. Research has shown that insulin-secretagogue therapy substantially increases the rate of SH compared to

insulin without secretagogues and secretagogues without insulin.(46)

Study strengths and limitations

This study evaluates a general, community-based cohort of Americans with diabetes—irrespective of infection status—to derive insight into the real-world, real-time consequences of the COVID-19 situation in diabetes. To mitigate selection bias, a broad sample of participants was recruited from a large, probability-based internet panel. Online data collection enabled us to capitalize on the high prevalence of internet use in the US,(47) while optimizing survey reach and accessibility, respondent honesty, and representativeness, as well as reducing item nonresponse.(48,49) Participant anonymity and confidentiality were assured to decrease the risk of social desirability bias.(50)

By developing a pandemic-specific questionnaire, our research team was able to elucidate the once unknown repercussions of the COVID-19 situation in Americans with diabetes; indeed, self-report data can offer unique and robust insight routinely uncaptured by other methods.

Though the study is cross-sectional in design, self-reported causal attributions of the pandemic were operationalized for each questionnaire item: respondents were asked to indicate to what extent "...the Coronavirus (COVID-19) situation [had] impacted" given aspects of glycemic management. Such information had yet to be garnered in the US.

Nevertheless, certain study limitations should be noted. Selection biases may have arisen to the extent that respondents differed non-randomly from the general US population with diabetes taking insulin and/or secretagogues. Specifically, survivorship and coverage bias (e.g., due to high observed percentages of Caucasian, educated, and insured participants) could have curtailed the external validity of results. Volunteer bias may have also led participants to over- or under-estimate their responses. For example, those who chose to complete the first COVID-19 sub-questionnaire may have possessed systemically different (positive or negative) pandemic-related perspectives and/or experiences than those who did not.

Estimates derived in our study may be conservative, as they stem from a one-month data capture in the early phase of the pandemic trajectory. In addition, self-reported responses could have been influenced by social desirability bias and/or recall error. Even so, self-report data—typically the Hobson's choice for information on perspectives, views, and opinions—enabled us to capture, for the first time, the impacts of COVID-19 on various socio-economic,

behavioural/clinical, and psychosocial aspects of diabetes management in the US. The results of our study (though not exhaustive, per se), provide important, unprecedented insight into the real-world fallouts of the pandemic situation on diabetes-related health.

Analyses of psychometric properties and/or adjusted frequency estimates were beyond the scope of this manuscript. Rather this study supplies descriptive, novel, and time-sensitive evidence at the convergence of COVID-19 and diabetes, contributing to both the national and international body of pandemic literature.

CONCLUSIONS

A 'hinterland' is defined as an area lying beyond what is visible or known. As a society we have exhibited unparalleled bravery in the face of one of the most terrifying crises known to humankind. However, our mission to abate the pandemic is only just beginning. Indeed, the COVID-19 calamity has had untold reverberations in the lives of Americans, extending well-beyond the visible devastations caused by infection alone. Not least are the impacts COVID-19 has had on PWD—cases and non-cases alike—who have struggled to maintain control of their disease amidst the pandemic.

Yet, until now, the nature and scale of these impacts in the US were largely unknown or uncharacterized. Thus, the results of our study draw not only awareness to the far-reaching and potential lasting consequences of the pandemic, but offer an evidence base for decisive action. In identifying the unique needs of Americans with diabetes during the COVID-19 era, we can begin to develop, implement, and assess clinical and public health strategies that ensure safe, undisrupted care within communities of people with diabetes. As we combat the acute phase of COVID-19, we must not lose sight of the pernicious health challenges that coexist and await us in the aftermath.

CONTRIBUTORSHIP STATEMENT: A.A.R.-L. contributed to the discussion, researched data, and wrote the manuscript. B.L.R. contributed to the discussion and reviewed/edited the manuscript. J.D.B. contributed to the discussion and reviewed/edited the manuscript. J.W.D. contributed to the discussion and reviewed/edited the manuscript. J.E.B. reviewed/edited the manuscript. S.B.H. contributed to the discussion, researched data, and reviewed/edited the manuscript.

GUARANTOR'S NAMES: Stewart B. Harris and Alexandria A. Ratzki-Leewing

TRANSPARENCY DELCARATION: S.B.H. affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have

been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

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Table 1. Socio-demographic characteristics of study sample, overall and by diabetes type

SOCIO-DEMOGRAPHIC CHARACTERISTICS	Total N=667	T1DM 120 (17.99%)	T2DM 547 (82.01%)
Age, mean (SD)			
Years	51.85 (14.57)	45.96 (14.43)	53.14 (14.29)
Age (categorical), n (%)			
≥ 18 and ≤ 40 years	180 (26.99)	51 (42.50)	129 (23.58)
≥ 41 and ≤ 64 years	332 (49.78)	53 (44.17)	279 (51.01)
≥ 65 and ≤ 74 years	123 (18.44)	11 (9.17)	112 (20.48)
≥ 75 years	32 (4.80)	5 (4.17)	27 (4.94)
Sex assigned at birth, n (%)			
Male	326 (48.88)	40 (33.33)	286 (52.29)
Female	341 (51.12)	80 (66.67)	261 (47.71)
Race, n (%)			
White	555 (83.21)	111 (92.50)	444 (81.17)
Black or African American	52 (7.80)	3 (2.50)	49 (8.96)
Asian	17 (2.55)	3 (2.50)	14 (2.56)
Hispanic, Latino/a, or Spanish origin	13 (1.95)	1 (0.83)	12 (2.19)
American Indian, Alaska Native, Native Hawaiian, or Pacific Islander	4 (0.60)	0	4 (0.73)

Multiracial	23 (3.45)	2 (1.67)	21 (3.84)
Other	3 (0.45)	0	3 (0.55)
Hispanic, Latino/a, or Spanish origin, n (%)			
Mexican, Mexican American, Chicano	27 (4.05)	2 (1.67)	25 (4.57)
Puerto Rican	6 (0.90)	1 (0.83)	5 (0.91)
Cuban	2 (0.30)	0	2 (0.37)
Other Hispanic, Latino/a, or Spanish origin	3 (0.45)	1 (0.83)	2 (0.37)
Not of Hispanic, Latino/a, or Spanish origin	629 (94.30)	116 (96.67)	513 (93.78)
Highest level of education, n (%)			
Elementary or high school (No diploma)	10 (1.50)	3 (2.50)	7 (1.28)
High school diploma or GED/alternative credential	101 (15.14)	19 (15.83)	82 (14.99)
College degree or some college	425 (63.72)	75 (62.50)	350 (63.99)
Degree beyond completing first college Bachelor's degree	131 (19.64)	23 (19.17)	108 (19.74)
Current employment status, n (%)			
Employed full-time or part-time (including self-employment)	346 (51.87)	73 (60.83)	273 (49.91)
Temporarily laid off/Temporarily unemployed due to a health issue	4 (0.60)	1 (0.83)	3 (0.55)
Unable to work due to disability	84 (12.59)	11 (9.17)	73 (13.35)
Unemployed	55 (8.25)	15 (12.50)	40 (7.31)
Student	4 (0.60)	1 (0.83)	3 (0.55)
Retired	174 (26.09)	19 (15.83)	155 (28.34)
Total annual household income (before taxes and deductions), n (%)			

<$24,999	107 (16.21)	13 (11.21)	94 (17.28)
$25,000 to $54,999	173 (26.21)	25 (21.55)	148 (27.21)
$55,000 to $84,999	142 (21.52)	39 (33.62)	103 (18.93)
$85,000 to $114,999	109 (16.52)	22 (18.97)	87 (15.99)
≥ $115,000	129 (19.55)	17 (14.66)	112 (20.59)
Current healthcare insurance, n (%)			
Insurance through a current or former employer or union that is not a high deductible plan†	153 (22.94)	36 (30.00)	117 (21.39)
Insurance purchased directly from an insurance company that is not a high deductible plan†	49 (7.35)	11 (9.17)	38 (6.95)
High deductible plan†	34 (5.10)	11 (9.17)	23 (4.20)
Medicare	77 (11.54)	7 (5.83)	70 (12.80)
Medicaid, Medical Assistance, or other government-assistance plan	74 (11.09)	17 (14.17)	57 (10.42)
TRICARE and Veterans Affairs	9 (1.35)	2 (1.67)	7 (1.28)
Other	5 (0.75)	2 (1.67)	3 (0.55)
Two or more insurance plans	257 (38.53)	32 (26.67)	225 (41.13)
No insurance coverage at all	9 (1.35)	2 (1.67)	7 (1.28)

T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; SD, standard deviation.

* Responses may not sum to total (N=667) due to missing data.

† High Deductible Plan: Deductible >$1,350 for an individual or >$2,700 for a family.

Table 2. Clinical characteristics of study sample, overall and by diabetes type

CLINICAL CHARACTERISTICS		Total	T1DM	T2DM
		N=667	120 (17.99%)	547 (82.01%)
Duration of diabetes, median (IQR)				
	Years	13 (15)	26 (23)	11 (14)
Most recent hemoglobin A1C, n (%)				
	≤ 7%	252 (37.78)	45 (37.50)	207 (37.84)
	7.1-8%	239 (35.83)	45 (37.50)	194 (35.47)
	8.1-9%	99 (14.84)	14 (11.67)	85 (15.54)
	≥ 9.1%	55 (8.25)	14 (11.67)	41 (7.50)
	Unsure	12 (1.80)	0	12 (2.19)
BMI at time of study enrolment, median (IQR)				
	BMI (kg/m^2)	30.38 (11.87)	26.43 (6.18)	32.19 (11.99)
Current insulin and/or secretagogue use, n (%)				
	Insulin *without* Secretagogues	330 (49.48)	120 (100.00)	210 (38.39)
	Secretagogues *without* Insulin	202 (30.28)	0	202 (36.93)
	Insulin *in combination with* Secretagogues	135 (20.24)	0	135 (24.68)
Diagnosed diabetes-related complications since 1 year preceding study enrolment, n (%)‡				

No complications	263 (39.43)	41 (34.17)	222 (40.59)
One or more complications	404 (60.57)	79 (65.83)	325 (59.41)
Amputation	91 (13.64)	12 (10.00)	79 (14.44)
Diabetes Ketoacidosis	110 (16.49)	42 (35.00)	68 (12.43)
Foot damage	123 (18.44)	18 (15.00)	105 (19.20)
Gastroparesis	95 (14.24)	20 (16.67)	75 (13.71)
Hyperosmolar hyperglycemic nonketotic coma	60 (9.00)	5 (4.17)	55 (10.05)
Nephropathy	114 (17.09)	18 (15.00)	96 (17.55)
Neuropathy	298 (44.68)	46 (38.33)	252 (46.07)
Retinopathy	156 (23.39)	46 (38.33)	110 (20.11)
Comorbidity status at time of study enrolment, n (%)‡			
No comorbidities	112 (16.79)	32 (26.67)	80 (14.63)
One or more comorbidities	555 (83.21)	88 (73.33)	467 (85.37)
Bone, joint, or muscle problem	310 (46.48)	39 (32.50)	271 (49.54)
Cancer	52 (7.80)	3 (2.50)	49 (8.96)
Cardiovascular condition	128 (19.19)	17 (14.17)	111 (20.29)
Chronic kidney disease	73 (10.94)	8 (6.67)	65 (11.88)
Chronic liver failure or liver disease	39 (5.85)	2 (1.67)	37 (6.76)
Eating disorder	35 (5.25)	7 (5.83)	28 (5.12)
Gastrointestinal disease	86 (12.89)	17 (14.17)	69 (12.61)
HIV/AIDS	11 (1.65)	2 (1.67)	9 (1.65)
Hypertension	363 (54.42)	50 (41.67)	313 (57.22)
Mental health condition	223 (33.43)	36 (30.00)	187 (34.19)
Neurological disorder	39 (5.85)	8 (6.67)	31 (5.67)

Physical impairment	168 (25.19)	29 (24.17)	139 (25.41)
Respiratory condition	125 (18.74)	24 (20.00)	101 (18.46)
Stroke or transient ischemic attack	44 (6.60)	5 (4.17)	39 (7.13)
Current continuous glucose monitoring device use, n (%)			
Yes	229 (34.33)	65 (54.17)	164 (29.98)

T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; IQR, interquartile range; BMI: body mass index.

* Responses may not sum to total (N=667) due to missing data.

‡ Cumulative percentage >100% as participants could select more than one response.

Table 3. Incidence rates and proportions of severe and non-severe hypoglycemia, overall and by diabetes type

INCIDENCE RATES*	Total N=667	T1DM 120 (17.99%)	T2DM 547 (82.01%)
Severe Hypoglycemia (one-month retrospective)			
Daytime + Nocturnal:			
Events per person-month (95% CI†)	0.68 (0.48 to 0.96)	0.39 (0.18 to 0.85)	0.75 (0.51 to 1.09)
Non-Severe Hypoglycemia (one-month retrospective)			
Daytime + Nocturnal:			
Events per person-month (95% CI†)	2.75 (2.43 to 3.11)	5.73 (4.60 to 7.13)	2.10 (1.82 to 2.41)
INCIDENCE PROPORTIONS*	**Total** N=667	**T1DM** 120 (17.99%)	**T2DM** 547 (82.01%)
Severe Hypoglycemia (one-month retrospective)			
Daytime or Nocturnal:			
% with ≥ 1 event (95% CI‡)	12.91 (10.58 to 15.67)	11.67 (7.078 to 18.63)	13.19 (10.6 to 16.28)
Non-Severe Hypoglycemia (one-month retrospective)			
Daytime or Nocturnal:			
% with ≥ 1 event (95% CI‡)	60.06 (56.29 to 63.71)	83.33 (75.66 to 88.94)	54.95 (50.75 to 59.07)

T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; CI, confidence interval.

* Incidence rates and proportions are based on data from participants who reported taking insulin and/or secretagogues at Month 2 follow-up.

† Based on Negative Binomial distribution.

‡ Based on Wilson Score Interval.

Table 4. Impact of the COVID-19 situation on aspects of participants' glycemic management (past month)*, overall and by diabetes type

	...has been **much harder**	...has been **somewhat harder**	...has **not** been impacted	... has been **somewhat easier**	... has been **much easier**	*P*-value†
Affording my rent and other living expenses...						
Overall (N=667)	59 (8.85)	103 (15.44)	491 (73.61)	12 (1.80)	2 (0.30)	
T1DM (n=120)	13 (10.83)	23 (19.17)	83 (69.17)	1 (0.83)	0	0.08
T2DM (n=547)	46 (8.41)	80 (14.63)	408 (74.59)	11 (2.01)	2 (0.37)	
Making sure I have enough food to avoid hypoglycemia...						
Overall (N=667)	54 (8.10)	130 (19.49)	475 (71.21)	7 (1.05)	1 (0.15)	
T1DM (n=120)	8 (6.67)	20 (16.67)	91 (75.83)	1 (0.83)	0	0.29
T2DM (n=547)	46 (8.41)	110 (20.11)	384 (70.20)	6 (1.10)	1 (0.18)	
Affording my diabetes medication(s)...						
Overall (N=667)	53 (7.95)	71 (10.64)	534 (80.06)	5 (0.75)	4 (0.60)	
T1DM (n=120)	10 (8.33)	10 (8.33)	99 (82.50)	1 (0.83)	0	0.71

T2DM (n=547)	43 (7.86)	61 (11.15)	435 (79.52)	4 (0.73)	4 (0.73)	
Affording my test strips and/or sensors...						
Overall (N=667)	42 (6.30)	74 (11.09)	540 (80.96)	5 (0.75)	6 (0.90)	
T1DM (n=120)	9 (7.50)	7 (5.83)	103 (85.83)	1 (0.83)	0	0.38
T2DM (n=547)	33 (6.03)	67 (12.25)	437 (79.89)	4 (0.73)	6 (1.10)	
Getting my diabetes medication(s) from the pharmacy...						
Overall (N=667)	58 (8.70)	125 (18.74)	470 (70.46)	8 (1.20)	6 (0.90)	
T1DM (n=120)	13 (10.83)	24 (20.00)	82 (68.33)	1 (0.83)	0	0.24
T2DM (n=547)	45 (8.23)	101 (18.46)	388 (70.93)	7 (1.28)	6 (1.10)	
Consulting with my healthcare provider(s) about my diabetes...						
Overall (N=667)	85 (12.74)	158 (23.69)	410 (61.47)	13 (1.95)	1 (0.15)	
T1DM (n=120)	14 (11.67)	28 (23.33)	76 (63.33)	2 (1.67)	0	0.75
T2DM (n=547)	71 (12.98)	130 (23.77)	334 (61.06)	11 (2.01)	1 (0.18)	
Testing/monitoring my blood glucose...						
Overall (N=667)	34 (5.10)	72 (10.79)	551 (82.61)	7 (1.05)	3 (0.45)	
T1DM (n=120)	4 (3.33)	2 (1.67)	110 (91.67)	4 (3.33)	0	<0.001‡
T2DM (n=547)	30 (5.48)	70 (12.80)	441 (80.62)	3 (0.55)	3 (0.55)	
Remembering to take my diabetes medication(s) as prescribed...						
Overall (N=667)	26 (3.90)	65 (9.75)	554 (83.06)	18 (2.70)	4 (0.60)	
T1DM (n=120)	1 (0.83)	7 (5.83)	109 (90.83)	3 (2.50)	0	0.047‡
T2DM (n=547)	25 (4.57)	58 (10.60)	445 (81.35)	15 (2.74)	4 (0.73)	
Monitoring my risk of hypoglycemia regularly...						
Overall (N=667)	29 (4.35)	51 (7.65)	561 (84.11)	23 (3.45)	3 (0.45)	0.026‡

T1DM (n=120)	3 (2.50)	6 (5.00)	103 (85.83)	8 (6.67)	0	
T2DM (n=547)	26 (4.75)	45 (8.23)	458 (83.73)	15 (2.74)	3 (0.55)	
Staying as physically active as I usually am...						
Overall (N=667)	100 (14.99)	209 (31.33)	329 (49.33)	23 (3.45)	6 (0.90)	
T1DM (n=120)	21 (17.50)	36 (30.00)	55 (45.83)	7 (5.83)	1 (0.83)	0.84
T2DM (n=547)	79 (14.44)	173 (31.63)	274 (50.09)	16 (2.93)	5 (0.91)	
Feeling in control of my hypoglycemia...						
Overall (N=667)	35 (5.25)	62 (9.30)	528 (79.16)	35 (5.25)	7 (1.05)	
T1DM (n=120)	5 (4.17)	9 (7.50)	99 (82.50)	6 (5.00)	1 (0.83)	0.50
T2DM (n=547)	30 (5.48)	53 (9.69)	429 (78.43)	29 (5.30)	6 (1.10)	
Having enough social support to help me manage my hypoglycemia...						
Overall (N=667)	41 (6.15)	83 (12.44)	518 (77.66)	21 (3.15)	4 (0.60)	
T1DM (n=120)	3 (2.50)	10 (8.33)	104 (86.67)	3 (2.50)	0	0.056
T2DM (n=547)	38 (6.95)	73 (13.35)	414 (75.69)	18 (3.29)	4 (0.73)	

T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus.

n (%) are presented.

* Data collected April 21st to 28th, 2020.

† Item responses were compared between individuals with T1DM and T2DM. *P*-values were computed using two-sample Wilcoxin-Mann-Whitney tests.

‡ Statistically significant at an alpha value of 0.05 (i.e., the underlying distributions of item responses statistically significantly differed by diabetes type).

Table 5. Impact of the COVID-19 situation on diabetes medication rationing (past month) *, overall and by diabetes type

	Total	T1DM	T2DM	
	N=667	120 (17.99%)	547 (82.01%)	*P*-value †
Rationed to make diabetes medication(s) supply last longer				
Yes	111 (16.64)	16 (13.33)	95 (17.37)	0.28
Rationed to avoid hypoglycemia				
Yes	112 (16.79)	19 (15.83)	93 (17.00)	0.76

T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus.

n (%) are presented.

* Data collected April 21st to 28th, 2020

† Item responses were compared between individuals with T1DM and T2DM. *P*-values were computed using two-sample Z tests for proportions.

Appendix A. Items assessing the impact of the COVID-19 situation on aspects of diabetes management

On a scale from *much harder* to *much easier*, please tell us how the Coronavirus (COVID-19) situation has impacted the following aspects of your life.

In general, **since the last time I completed an iNPHORM survey**...

		...has been much harder	...has been somewhat harder	...has **not** been impacted	... has been somewhat easier	...has been much easier
1.	...Affording my rent and other living expenses	☐	☐	☐	☐	☐
2.	...Affording my diabetes medication(s)	☐	☐	☐	☐	☐
3.	...Affording my test strips and/or sensors	☐	☐	☐	☐	☐
4.	...Getting my diabetes medication(s) from the pharmacy	☐	☐	☐	☐	☐
5.	...Making sure I have enough food to avoid hypoglycemia	☐	☐	☐	☐	☐
6.	...Testing/monitoring my blood glucose	☐	☐	☐	☐	☐
7.	...Staying as physically active as I usually am	☐	☐	☐	☐	☐
8.	...Consulting with my healthcare provider(s) about my diabetes	☐	☐	☐	☐	☐
9.	...Remembering to take my diabetes medication(s) as prescribed	☐	☐	☐	☐	☐
10.	...Monitoring my risk of hypoglycemia regularly	☐	☐	☐	☐	☐
11.	...Having enough social support to help me manage my hypoglycemia	☐	☐	☐	☐	☐
12.	...Feeling in control of my hypoglycemia	☐	☐	☐	☐	☐

When answering this next question, please think about the time **since you last completed an iNPHORM survey**.

Because of the Coronavirus (*COVID-19)* situation, did you ever **cut back** on your diabetes medication(s) in order to...

	Yes	No
13. ...make your diabetes medication(s) supply last longer?	☐	☐
14. ...avoid hypoglycemia?	☐	☐

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page # (line #)
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 (lines 3-4)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Pages 3 and 4 (lines 1-6)
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pages 4 (lines 20-22), 5 (lines 1-10), 7 (lines 9-22), and 8 (lines 1-2)
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 8 (lines 3-8)
Methods			
Study design	4	Present key elements of study design early in the paper	Pages 8 (lines 14-23) and 9 (all)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 8 (line 17) and 9 (line 22)
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Pages 8 (lines 21-23) 9 (lines 4-7)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pages 10 and 11 (lines 1-18)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pages 10 (lines 3-6 and 20-23), 11 (lines 1-6, 8, 11-14), 40, and 41
Bias	9	Describe any efforts to address potential sources of bias	Pages 22 and 23 (lines 1-12)
Study size	10	Explain how the study size was arrived at	Pages 8 (lines 21-23) and 9 (lines 1-22)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pages 10 (lines 1-23) and 11 (lines 1-18)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Pages 11 (lines 20-23) and12 (lines 1-8)

		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	Page 12 (lines 7-8)
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Page 8 (lines 21-23)
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Pages 8 (lines 21-23); 9 (lines 1-10); 12 (lines 22-23) and 10 (lines 1-11).
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Pages 12 (lines 22-23) and 12 (lines 1-11). Also Table 1 page 33-34
		(b) Indicate number of participants with missing data for each variable of interest	Tables 1, 2, 3, 4
Outcome data	15*	Report numbers of outcome events or summary measures	Pages 12 (lines 22-23); 13 (1-21); 14 (1-23); 15 (1-23); and 16 (1-4)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Pages 13 (lines 12-21); 14 (lines 1-23); 15 (lines 1-23); and 16 (lines 1-4)
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	Pages 16 (lines 8 -21); 17 (lines 1-23); 18 (lines 1-23);

			19 (lines 1-23); 20 (lines 1-23); 21 (lines 1-23); 22 (lines 1-23); and 23 (lines 1-12)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Pages 22 (lines 16-23) and 23 (lines 1-12)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Pages 16 (lines 8 -21); 17 (lines 1-23); 18 (lines 1-23); 19 (lines 1-23); 20 (lines 1-23); 21 (lines 1-23); 22 (lines 1-23); and 23 (lines 1-12)
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 22 (line 18-20)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 24 (lines 16-17)

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.