

# Patient Portal Use Among Diabetic Patients With Different Races and Ethnicities

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## Abstract

**Background:** Patient portal (PP) use varies among different patient populations, specifically among those with diabetes mellitus (DM). In addition, it is still uncertain whether PP use could be linked to improved clinical outcomes. Therefore, the aim of this paper was to determine PP use status for patients, recognize factors promoting PP use, and further identify the association between PP use and clinical outcome among diabetic patients of different races and ethnicities.

**Methods:** This was a single-center cross-section study. Patients were divided into non-Hispanic white (NHW), non-Hispanic black (NHB), and Hispanic/Latino groups. PP use was compared among these three groups. Multivariate logistic regressions were used to determine factors associated with PP use, serum glycemic control, and emergency department (ED) hospitalizations.

**Results:** A total of 77,977 patients were analyzed. The rate of PP use among patients of NHW (24%) was higher than those of NHB (19%) and Hispanic/Latinos (18%, P < 0.0001). The adjusted odds ratio (AOR) of insurance coverage associated with PP use was 2.12 (2.02 - 2.23, P < 0.0001), and having a primary care physician (PCP) associated with PP use was 3.89 (3.71 - 4.07, P < 0.0001). In terms of clinical outcomes, the AOR of PP use associated with serum glycemic control was 0.98 (0.90 - 1.05, P = 0.547) and ED hospitalization was 0.79 (0.73 - 0.86, P < 0.0001).

**Conclusion:** PP use disparity occurred among NHB and Hispanic/ Latino patients in the ED. Having insurance coverage and PCPs seem to correlate with PP use. PP use did not seem to associate with serum glycemic control among DM patients present in the ED but could possibly reduce patient hospitalizations.

Keywords: Patient portal; Diabetes mellitus; Races; Ethnicities

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## Introduction

Personal health records (PHR) tethered to patient electronic medical records (i.e., patient portals (PPs)) have been introduced to patients for decades [1, 2]. PP has many features and allows patients to have better communication with their healthcare providers, request refills for their medications, and arrange their clinic follow-ups. In short, it is a tool that allows patients to have better patient-healthcare connections [1, 3-5].

In previous reports, PP use has been increasing in recent years among patients with chronic conditions, especially those with diabetes mellitus (DM) [1, 6]. Some studies depict that 32-40% of patients with DM have adopted portal accounts in their healthcare systems [6, 7]. However, the digital divide occurred among patients of different races/ethnicities [8], and studies show that PP usage has not increased evenly across demographics in those with DM [6]. Patients who live in rural areas with low income, and nonwhites with low income were less likely to access their PP [6]. Similarly, non-Hispanic black (NHB) were less likely to register their PP compared to their non-Hispanic white (NHW) counterparts [9]. However, these studies either had relatively small sample sizes; or the populations of different races/ethnicities were not well balanced (e.g., different sample sizes compared among NHW, NHB, or Hispanic/Latinos). Additionally, PP use disparities occurred more often among patients with chronic conditions. Previous studies focused more on the report of their PP use among patients with DM, whereas few studies reported PP use status among patients with other chronic conditions [7, 10, 11]. To address this literature gap, it is necessary to determine PP use status among different races/ethnicities using a well-balanced patient sample in the same healthcare environment. Meanwhile, it is also important to determine PP use status among patients with DM in comparison to those with other chronic conditions.

When reviewing the literature, PP use in those with DM has been linked to improved healthcare outcomes [12, 13]. The use of PP has been significantly associated with better serum glycemic control [6, 14, 15]. Similarly it has been found that patients who use their PP more frequently, and for longer periods of time, are likely to have better clinical outcomes than those who use it less often [16, 17]. PP use for patients with DM who have multiple medical conditions has also been associated with significantly higher rates of outpatient office visits, fewer emergency department (ED) visits, and preventative hospital stays [11]. However, these clinical outcomes have rarely been

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This article is distributed under the terms of the Creative Commons Attribution Non-Commercial 4.0 International License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited compared among diabetic patients of different races/ethnicities, especially in an acute care setting.

There are many barriers and facilitators that play a role in PP use [18-20]. Determining the current PP use status among patients of different races/ethnicities and identifying promoting factors of PP use may help patients gain better healthcare connections, improve self-care management of chronic diseases, and eventually improve patient healthcare outcomes [21-23]. Therefore, we aim to determine: 1) the PP use status, 2) the PP use associated with clinical outcomes (serum glycemic control and hospitalization), and 3) potential facilitators of PP use among diabetic patients of different races and ethnicities.

## **Materials and Methods**

#### Study design and setting

This was a single-center retrospective cross-sectional study. The study hospital is a publicly funded hospital with one ED. An electronic medical record (Epic) and a tethered PP (My-Chart) have been implemented in the study healthcare system since 2012. All patients within the study healthcare system have access to their MyChart. MyChart has many features similar to other PPs. The main features are: 1) refill medications, 2) check lab and image results, 3) pay healthcare costs, 4) arrange clinical appointments, and 5) communicate with healthcare providers. The hospital ED has annual patient visits of approximately 120,000. The ED has patients of various racial and ethnic backgrounds including approximately one-third of NHW, one-third of NHB, and another third of Hispanic/Latino patients. The study procedure was designed in compliance with the Declaration of Helsinki. This study was approved by the institution's respective Institutional Review Board with waived informed consent due to its retrospective study and deidentified data (No. 1600198-5).

#### Study participants

Patients who visited the ED at least once from March 1, 2019 to February 28, 2021 were included. In this study, we intended to determine patient PP use status upon their indexed ED visits. Therefore, we only included patients who had visited the study healthcare system before their indexed ED visits. This would ensure that our participants had access to their PP prior to their indexed ED visits. In addition, if patients had multiple ED encounters during the study period, we only investigated patients' latest PP status (i.e., all variables were extracted from the last recorded visit during the study period). Patients' chronic conditions were identified and multimorbidity was defined as the presence of two or more chronic conditions based on Goodman's criteria [24]. Additionally, this study mainly focused on the comparisons of NHW, NHB, and Hispanic/Latino patient populations. Since our ED patients of other races (e.g., American Native Indian, Alaska Natives, Hawaiian, and other Pacific Islanders, etc.) only accounted for approximately 6% of the entire study cohort, we further excluded those in our

final analyses. A detailed study flow of the patient selection is shown in Figure 1.

#### Variables

#### Dependent variable

The primary outcome was to determine PP use (yes/no): ED patients who signed on to their MyChart account at least once within 12 months prior to their indexed ED visit were considered positive PP users. If patients did not log on to their My-Chart in the past 12 months, we considered them to be negative PP users. Our secondary outcome was to determine DM patient clinical outcomes including serum glycemic control upon patient presenting to the ED triage (i.e., serum glucose level). At ED triage, a serum glucose measurement was performed in patients with a history of DM regardless of their chief complaints. Similarly, if patients were brought in by ambulance, a bedside serum glucose check was also performed on each diabetic patient. Additionally, patient hospitalization was tracked as a secondary outcome.

#### Key explanatory variables

Patient demographic variables included age, sex (male and female), preferred language (English, Spanish, and others), and race/ethnicity. We divided race/ethnicity into three groups: NHW, NHB, and Hispanic/Latino. In addition, patients' other healthcare information included insurance status (yes or no), and whether patients had a primary care physician (PCP) (yes or no).

#### Statistical analyses

Continuous data were summarized as: 1) means  $\pm$  standard deviation (SD) and compared using analysis of variance (ANOVA); and 2) medians (interquartile ranges (IQRs)) and compared using Wilcoxon rank sum test between groups. Categorical data were summarized by frequencies and percentages and compared using the Chi-squared test among groups. Then, a multivariate logistic regression was performed to determine the association between different races/ethnicities and PP use, and further identify factors promoting PP use. Similarly, the associations of PP use and serum glycemic control and hospitalizations were also analyzed using multivariate logistic regression models. All these logistic regressions were analyzed with the adjustment of patient age, sex, race/ethnicity, language, insurance coverage, and having PCPs. Adjusted odds ratios (AORs) were reported with 95% confidence intervals (CIs). Investigators used STATA 14.2 (College Station, TX) for all statistical study analyses, with P < 0.05considered statistically significant.

#### **Reporting guideline**

This study was reported using the Strengthening of the Re-

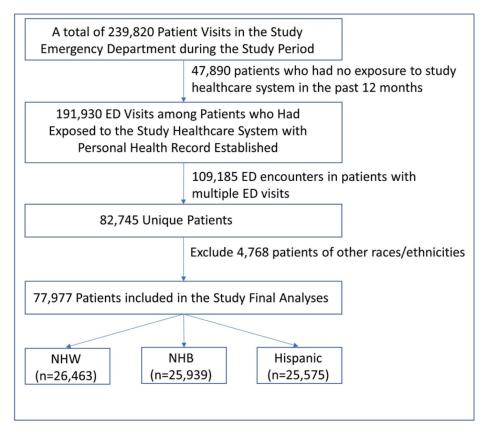


Figure 1. Study flow diagram.

porting of Observational Studies in Epidemiology (STROBE) reporting guidelines [25].

## Results

In this study, after excluding patients who did not have previous exposure to the study healthcare system with no PP access, we found 82,745 unique patients met the inclusion criteria during the study period. After further exclusion of 4,768 patients of other races/ethnicities, a total of 77,977 unique patients were placed in our final analysis, among which 26,463 patients (34%) were NHW, 25,939 patients (33%) were NHB, and 25,575 patients (33%) were Hispanic/Latinos. Therefore, well-balanced patient populations of three different races/ethnicities were achieved. A detailed study flow diagram is shown in Figure 1.

Table 1 shows the baseline characteristics of the study patients. We divided all patients into three groups. The rate of PP use among patients of NHW was higher than those of NHB and Hispanic/Latinos (P < 0.0001). Additionally, NHB and Hispanic/Latino patients tended to be female predominant, and younger than NHWs (P < 0.0001). Hispanic/Latino patients had less insurance coverage than NHW and NHB, whereas NHB patients had less PCPs than NHW and Hispanic/Latinos (P < 0.0001). In terms of chronic conditions, the top nine common chronic conditions are listed in Table 1. NHB and Hispanic/Latino patients had a higher occurrence of DM than NHW, whereas NHW had a higher occurrence of depression, asthma/chronic obstructive pulmonary disease (COPD), and coronary artery disease (CAD)/congestive heart failure (CHF) than NHB and Hispanic/Latino (Table 1).

Since one of this study's foci was determining PP status in patients with DM, we further divided patients into five groups (group 1: patients with no chronic disease, group 2: patients with only a history of DM, group 3: patients with one chronic condition but not DM, group 4: patients with multimorbidity including DM, and group 5: patients with multimorbidity without DM). We found that only 1.3% (1,041/77,977) patients had DM as their only chronic condition. The PP use rate increased with the addition of chronic conditions regardless of patient races/ethnicities (Table 2). In general, more PP users were found in NHW patients than NHB and Hispanic/Latino patients.

When determining factors associated with PP use, a multivariate logistic regression was performed. The AOR of NHB with PP use was 0.61 (95% CI: 0.58 - 0.64, P < 0.0001) and the AOR of Hispanic/Latino with PP use was 0.91 (0.86 - 0.96, P < 0.0001) in comparison to PP use among NHWs. These findings indicate the lack of PP usage among NHB and Hispanic/Latino patients. Additionally, increased PP use occurred with the increased number of patients' chronic conditions, and such a trend occurred among patients with any chronic conditions. These findings indicate that DM is not the only chronic disease

Table 1.	Description	of the Study Population	(N = 77,977)
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	NHW	NHB	Hispanic/Latino	P value
Number of patients (n)	26,463	25,939	25,575	
Patient portal use (n, %)				< 0.0001
No	20,043 (76)	21,008 (81)	21,026 (82)	
Yes	6,420 (24)	4,931 (19)	4,549 (18)	
Age (years)				
Mean (SD)	46 (16)	44 (16)	43 (17)	< 0.0001
Median (IQR)	47 (33 - 58)	43 (30 - 57)	41 (29 - 55)	< 0.0001*
Sex (n, %)				< 0.0001
Male	13,995 (53)	12,692 (49)	11,820 (46)	
Female	12,467 (47)	13,247 (51)	13,754 (54)	
Language spoken (n, %)				< 0.0001
English	26,198 (99)	24,969 (96)	14,988 (59)	
Spanish	62 (0.2)	8 (0.03)	10,505 (41)	
Others	203 (0.8)	962 (3.7)	82 (0.3)	
Insurance coverage (n, %)				< 0.0001
Yes	17,841 (67)	17,800 (69)	14,304 (56)	
No	8,594 (33)	8,116 (31)	11,247 (44)	
Has primary care physician (n, %)				< 0.0001
Yes	13,733 (52)	15,231 (59)	12,885 (50)	
No	12,730 (48)	10,708 (41)	12,690 (50)	
History of diabetes (yes) n, %	5,221 (20)	5,974 (23)	7,028 (27)	< 0.0001
History of hypertension (yes) n, %	11,589 (44)	13,239 (51)	9,671 (38)	< 0.0001
History of back pain (yes) n, %	5,419 (20)	6,029 (23)	4,300 (17)	< 0.0001
History of headache (yes) n, %	4,027 (15)	4,594 (18)	4,125 (16)	< 0.0001
History of asthma/COPD (yes) n, %	6,124 (23)	5,383 (21)	2,561 (10)	< 0.0001
History of hyperlipidemia (yes) n, %	5,735 (22)	5,383 (21)	5,306 (21)	0.011
History of obesity (yes) n, %	5,086 (19)	4,946 (19)	5,131 (20)	0.009
History of depression (yes) n, %	10,963 (41)	7,370 (28)	5,708 (22)	< 0.0001
History of CAD/CHF (yes) n, %	4,368 (17)	3,966 (15)	2,596 (10)	< 0.0001

\*P < 0.0001 (group 1 vs. group 2, group 1 vs. group 3, and group 2 vs. group 3). SD: standard deviation; IQR: interquartile range; NHB: non-Hispanic black; NHW: non-Hispanic white; COPD: chronic obstructive pulmonary disease; CAD: coronary artery disease; CHF: congestive heart failure.

promoting the use of PP (Table 3). We also found that females tended to use PP more often than males (AOR = 2.09, 95% CI: 2.01 - 2.17, P < 0.0001). The AOR of insurance coverage was 2.12 (2.02 - 2.23, P < 0.0001) and having a PCP was 3.89 (3.71 - 4.07, P < 0.0001), indicating these two independent factors potentially promoting PP usage (Table 3).

To further determine the association of PP use and patient clinical outcomes, a sub-cohort analysis was performed in DM patients. Blood serum glucose level and patient hospitalization were considered as two outcome measures. After adjusting for age, sex, race/ethnicity, language spoken, insurance coverage, PCP, and patient chronic conditions, PP use was not associated with better serum glycemic control (AOR = 0.98, P = 0.547). However, PP use was associated with significant reduction of patient hospitalization (AOR = 0.79, P < 0.0001, Table 4).

#### Discussion

To determine healthcare disparity in PP use, we performed a comparison study among three patient populations (i.e., NHW, NHB, and Hispanic/Latino) within the same healthcare environment. We found healthcare disparities still exist with PP use in NHB and Hispanic/Latino patients when compared to their NHW counterparts. Such disparity not only occurred among patients with DM but extended to patients with other chronic conditions. Meanwhile, being a female, having insurance coverage, and having PCPs positively correlated to patient PP usage. When focused on patients with DM, our findings show no association between PP use and serum glycemic control. However, our results show that patients who used PP had less hospitaliza-

	NHW	NHB	Hispanic/Latino	P value
Group 1: patients with no chronic disease (n = 16,177)				
Number of patients, n	4,549	4,868	6,760	
PP use (n, %)				0.001
Yes	455 (10)	516 (11)	581 (9)	
No	4,094 (90)	4,352 (89)	6,179 (91)	
Group 2: patients with only a history of DM $(n = 1,041)$				
Number of patients, n	189	209	643	
PP use (n, %)				0.004
Yes	29 (15)	41 (20)	70 (11)	
No	160 (85)	168 (80)	573 (89)	
Group 3: patients with one chronic disease but not DM ( $n = 14,988$ )				
Number of patients (n)	4,877	4,905	5,206	
PP use (n, %)				0.001
Yes	851 (17)	762 (16)	767 (15)	
No	4,026 (83)	4,143 (84)	4,439 (85)	
Group 4: patients with multimorbidity including a history of DM $(n = 17,182)$				
Number of patients (n)	5,032	5,765	6,385	
PP use (n, %)				< 0.000
Yes	1,784 (35)	1,432 (25)	1,544 (24)	
No	3,248 (65)	4,333 (75)	4,841 (76)	
Group 5: patients with multimorbidity without a history of DM ( $n = 28,589$ )				
Number of patients (n)	11,816	10,192	6,581	
PP use (n, %)				< 0.000
Yes	3,301 (28)	2,180 (21)	1,587 (24)	
No	8,515 (72)	8,012 (79)	4,994 (76)	

 Table 2.
 Patient PP Use Among ED Patients With Different Races/Ethnicities

ED: emergency department; PP: patient portal; DM: diabetes mellitus.

tions in comparison to ones not using PP. Our study used wellbalanced patient populations (i.e., similar sample size in NHW, NHB, and Hispanic/Latino) within the same healthcare system, determined the existence of PP use disparity among NHB and Hispanic/Latinos, and further identified factors promoting PP use. Our study findings contributed in several important areas to the literature pool: 1) a direct comparison of three common patient populations with relatively large sample size, 2) not only focusing on patients with DM but analyzing patients with other common chronic health conditions, and 3) determined PP status in an acute care setting instead of clinical setting, where PP use is not often emphasized. Our study findings could serve as a foundation for future implantation of efficient interventions to promote PP use, especially at an acute care setting.

PP use disparity has been reported in the past [6, 9, 26]. Our findings show similar results and validate the current PP use disparity among NHB and Hispanic/Latino patients, with a more robust sample population [26]. Many factors could be associated with such disparities, including low socioeconomic status (SES), education level, or internet access [10, 27, 28]. These factors have been reported and validated in the past. Therefore,

our study avoids such redundancies. Instead, we focused on potential factors that can be promoted by healthcare providers. Our findings showed insurance coverage and having a PCP are two factors promoting PP use. Though similar findings were reported in the past, it was reported from a national representative survey with no emphasis on patients with different races/ethnicities, nor focus on patients with DM [20]. Our study validated facilitators that may affect PP use regardless of patient race/ethnicity. Implementations to increase insurance coverage by providing hospital sponsored insurance coverage and increasing the referrals to PCPs by case managers in the study hospital have been initiated and showed certain improvement [29].

Strikingly, we did not find any association between PP use and patient serum glycemic control. Previous studies showed better DM control with the use of PP [6, 13]. However, these studies were either performed outside of an acute care setting or occurred as survey questionnaires [6, 13]. Furthermore, the high serum glucose levels might be affected by multiple factors including infection, medication interactions, stress, etc. [30-32]. DM patients might present to the ED due to other acute conditions unrelated to their DM, which might indirectly cause the

	AOR	95% CI	P value
Age	0.99	0.98 - 0.99	< 0.0001
Sex			
Male	Reference	Reference	
Female	2.09	2.01 - 2.17	< 0.0001
Race/ethnicity			
NHW	Reference	Reference	
NHB	0.61	0.58 - 0.64	< 0.0001
Hispanic/Latino	0.91	0.86 - 0.96	< 0.0001
Language speaking			
English	Reference	Reference	
Spanish	0.40	0.37 - 0.43	< 0.0001
Other languages	0.64	0.55 - 0.76	< 0.0001
Primary care physicians			
No	Reference	Reference	
Yes	3.89	3.71 - 4.07	< 0.0001
Insurance coverage			
No	Reference	Reference	
Yes	2.12	2.02 - 2.23	< 0.0001
Chronic disease condition			
No chronic disease	Reference	Reference	
Only history of DM	1.34	1.10 - 1.64	0.004
One chronic disease without DM	1.45	1.35 - 1.56	< 0.0001
Multimorbidity with DM	2.43	2.26 - 2.61	< 0.0001
Multimorbidity without DM	2.06	1.93 - 2.20	< 0.0001

Table 3. Factors Associated With PP Use Among ED Patients

AOR: adjusted odds ratio; CI: confidence interval; ED: emergency department; PP: patient portal; DM: diabetes mellitus; NHB: non-Hispanic black; NHW: non-Hispanic white.

elevation of serum glucose levels. We did not analyze patients' HbA1c level since this is not a routine test ordered in the ED. Given the potential for many confounding factors which can result in the elevation of serum glucose, we believe using HbA1c as the outcome measure may be better for determining such an association. On the other hand, this study also found that patients using PP had less hospitalizations. This may indicate that establishing patient-provider communication could avoid unnecessary hospitalizations. There are many PP features that could enhance patient-provider communication. If ED physicians recognized these resources, they may feel less pressure to admit patients especially among patients with high psychosocial risks. However, our study findings did not have direct evidence to support this hypothesis and future research is warranted for such validations.

Our study has the strength of a relatively large sample size with balanced patient populations. In addition, factors promoting the PP use determined in this study are feasible interventions that could be initiated instantly. Our future study will be to determine PP use with these interventions and further determine the association between PP use and patient clinical outcomes using better outcome indicators. Since such interventions can be applied to any patient populations, PP use disparity might thus be minimized.

This study has its limitations. First, since this is a retrospective cross-section study, incomplete, inaccurate, or missing data cannot be completely avoided. Due to data from a single healthcare system, we are unable to determine PP use status outside of our system. However, as the study hospital is the only publicly funded hospital in the county and most of the patient population received benefit from seeking healthcare in the study hospital (e.g., with hospital sponsored health insurance coverage, robust case management and social work network within the study healthcare system, etc.), we assume that very few patients would seek care from outside healthcare systems. Second, MyChart is one of the PPs that was investigated in our study. Since different PPs in different electronic medical records might have different features, our study findings might only reflect ones using MyChart and may not be generalizable. Future studies focusing on different PPs should be performed to validate our findings. Third, we were unable to include all variables that could affect PP use. We avoided choosing variables that have already been well

	AOR wit	AOR with 95% CI, P value	
	Serum glycemic control (normal vs. abnormal serum glucose)	ED disposition (no hospitaliza- tion vs. hospitalization)	
Serum glucose upon ED arrival		D.C.	
Normal		Reference	
Abnormal PP use		1.17 (1.09 - 1.25), P < 0.0001	
		D.C.	
No PP use	Reference	Reference	
PP use	0.98 (0.90 - 1.05), P = 0.547	0.79 (0.73 - 0.86), P < 0.0001	
Age	0.99 (0.98 - 0.99), P < 0.0001	1.03 (1.02 - 1.03), P < 0.0001	
Sex			
Male	Reference	Reference	
Female	0.86 (0.81 - 0.92), P < 0.0001	0.65 (0.61 - 0.70), P < 0.0001	
Race/ethnicity			
NHW	Reference	Reference	
NHB	0.85 (0.78 - 0.93), P < 0.0001	0.80 (0.74 - 0.87), P < 0.0001	
Hispanic/Latino	1.12 (1.02 - 1.23), P = 0.016	0.82 (0.74 - 0.90), P < 0.0001	
Language speaking			
English	Reference	Reference	
Spanish	1.02 (0.92 - 1.13), P = 0.692	1.08 (0.97 - 1.20), P = 0.177	
Other languages	1.09 (0.83 - 1.43), P = 0.521	0.66 (0.49 - 0.88), P = 0.005	
Primary care physicians			
No	Reference	Reference	
Yes	1.03 (0.95 - 1.11), P = 0.504	0.58 (0.53 - 0.63), P < 0.0001	
Insurance coverage			
No	Reference	Reference	
Yes	0.82 (0.75 - 0.89), P < 0.0001	1.65 (1.51 - 1.81), P < 0.0001	
Chronic disease condition			
Only history of DM	Reference	Reference	
Multimorbidity with DM	0.67(0.58 - 0.78), P < 0.0001	2.16 (1.82 - 2.58), P < 0.0001	

## Table 4. Factors Associated With Serum Glycemic Control and ED Disposition Among Diabetic Patients

AOR: adjusted odds ratio; CI: confidence interval; ED: emergency department; PP: patient portal; DM: diabetes mellitus; NHB: non-Hispanic black; NHW: non-Hispanic white.

validated in previous studies, although this could lead to some bias in the statistical analyses. Fourth, as mentioned above, we chose serum glucose level as one of the outcome measures, which might not be an accurate representation of serum glycemic control. Fifth, since our study hospital is a publicly funded hospital with special vulnerable patient populations, our findings might only be applied to patients in a similar setting. Therefore, a prospective multi-center study is warranted to further validate our findings.

#### Conclusion

PP use disparity occurred among NHB and Hispanic/Latino

patients in the ED. Having insurance coverage and a PCP was associated with increased PP use. PP use was not associated with serum glycemic control in DM patients presenting to the ED but could possibly reduce patient hospitalizations.

# Acknowledgments

None to declare.

# **Financial Disclosure**

None to declare.

# **Conflict of Interest**

None to declare.

# **Informed Consent**

This is waived by regional institution review board.

## **Author Contributions**

Conceptualization: HW, RK, AFH, and CDS. Methodology: HW, AP, and MB. Validation: AP, MB, and JB. Formal analysis: HW, RK, and CDS. Data curation: HW and RK. Writing original draft preparation: HW and RK. Writing review and editing: HW, RK, AP, MB, AFH, JB, and CDS.

# **Data Availability**

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

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