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Glucagon Use by U.S. Adults with Type 1 and Type 2 Diabetes

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Abstract

The American Diabetes Association recommends that all patients at risk for hypoglycemia be prescribed glucagon. Despite this recommendation, there is evidence that prescription rates are lower than expected for patients with type 1 and type 2 diabetes. This study investigated prescription patterns for glucagon among de-identified administrative claims from OptumLabs® Data Warehouse for prescriptions between January 1, 2014 and December 31, 2014 among pharmacologically treated type 1 and 2 diabetes patients. We find that glucagon was rarely filled by patients with type 1 and type 2 diabetes, including fewer than 5% of patients with prior hypoglycemia requiring emergency healthcare utilization. Among patients with type 1 diabetes, glucagon fills were unpredictable and not targeted to highest risk patients.

Introduction:

Severe hypoglycemia can be fatal if left untreated and results in nearly 300,000 emergency department (ED) visits in the U.S. annually, with an average cost of $1387 per visit.[1–3] When hypoglycemia does not respond to oral glucose, or results in loss of consciousness, it should be treated with glucagon. The American Diabetes Association recommends that all

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patients at risk for hypoglycemia be prescribed glucagon.[4] We sought to understand factors associated with filling glucagon prescriptions among privately insured adults with diabetes. We hypothesized that glucagon use is associated with prior hypoglycemic events, insulin use, and tighter glycemic control.

Methods:

This study used de-identified administrative claims from OptumLabs® Data Warehouse (OLDW), including medical and pharmacy claims and laboratory results (for a subset of the population) for commercial and Medicare Advantage enrollees.[5] Glucagon use was based on prescriptions filled between January 1, 2014 and December 31, 2014 among pharmacologically treated type 1 and 2 diabetes patients. Type 1 diabetes was based on use of insulin and claims for type 1 diabetes; type 2 diabetes was based on claims for type 2 diabetes. When mixed codes were present, type 1 diabetes was based on more claims for type 1 than for type 2 diabetes, and no fills for non-insulin glucose-lowering medications; all other patients were classified as type 2 diabetes. We excluded patients without pharmacy benefits coverage (n=132,275, 21.9%), without fills for a glucose-lowering medication in the 6 months prior to January 1, 2014 (n=134,421, 22.3%) and those with indeterminate type of diabetes (n=1,576, 0.3%). We examined association of glucagon fills with demographic, clinical (glucose-lowering medications from past 6 months, comorbidities and visits with endocrinologist from past 12 months) and laboratory-based (most recent hemoglobin A1c (HbA1c) available on a subset of patients) factors. Model performance was assessed with AUC and calibration plots. Analyses were performed using SAS. Study data were accessed using techniques adherent to the Health Insurance Portability and Accountability Act of 1996, and because this study involved analysis of preexisting, de-identified data, it was deemed exempt from institutional review board review.

Results:

Among 12,338 patients with type 1 and 323,244 with type 2 diabetes included in the study, 1.21% filled glucagon in 2014 (1.45% of patients with type 1 diabetes and 0.70% of patients with type 2 diabetes). Patients with type 1 diabetes who filled glucagon were more likely to be younger, female, white, have higher income, visit with an endocrinologist, prior ED/hospitalizations for any cause, and prior severe hypoglycemia compared with patients who did not fill glucagon (Table). However, the multivariable model had poor discriminative performance (AUC = 0.61); after adjustment, factors significantly associated with glucagon fills included age, sex, income, prior ED visits for any cause, and visit with an endocrinologist. Patients with type 2 diabetes who filled glucagon were more likely to be younger, female, white, have higher income, greater comorbidity burden, use insulin, have poor glycemic control, visit with an endocrinologist, prior ED/hospitalizations for any cause, and prior hypoglycemia compared with patients who did not fill glucagon (Table). Among patients with type 2 diabetes, the multivariable model had excellent discriminative performance (AUC = 0.89); after adjustment, factors significantly associated with glucagon use included age, race, household income, insulin regimen, prior hypoglycemia requiring ED/hospital care, and endocrinologist visit (Figure). HbA1c level was not independently associated with glucagon use in either type 1 or type 2 diabetes patients.

Discussion:

Glucagon is an evidence-based, guideline-recommended, and potentially life-saving medication for patients who experience severe hypoglycemia. In this national study, glucagon was rarely filled by patients with type 1 and type 2 diabetes, including fewer than 5% of patients with prior hypoglycemia requiring emergency healthcare utilization. Among patients with type 1 diabetes, glucagon fills were unpredictable and not targeted to highest risk patients. Unexplained variation in glucagon prescribing and use warrants further investigation; it is possible that it is driven by other, unmeasured factors or that it depends on clinician-specific practices. These unmeasured factors may include optimism bias, cost-effectives concerns, or other variation that has yet to be studied. In contrast, patients with type 2 diabetes were more likely to fill glucagon in the setting of insulin use and prior hypoglycemia. Taken together, these findings suggest opportunities to improve care, including better prescribing practices to target high-risk patients, particularly those with type 1 diabetes.

There are some limitations. OLDW includes commercially insured and Medicare Advantage patients, and findings may not generalize to uninsured patients or those covered by other plans. The data used in our study from 2014 may not be fully reflective of current practice patterns. We could not capture other factors affecting glucagon fills, including home support for glucagon administration or hypoglycemic episodes outside of ED/hospital.

Until recently, glucagon was only available as an intramuscular injection kit which needed to be reconstituted and refilled annually. Approval of easier-to-use glucagon preparations, such as the pre-filled syringes and nasal spray[6,7], may facilitate wider use but cost remains high (retail price ~$300 per device). Future work should identify patient, clinician, and system level barriers to glucagon use in order to improve care.

Conflict of Interest Disclosures:

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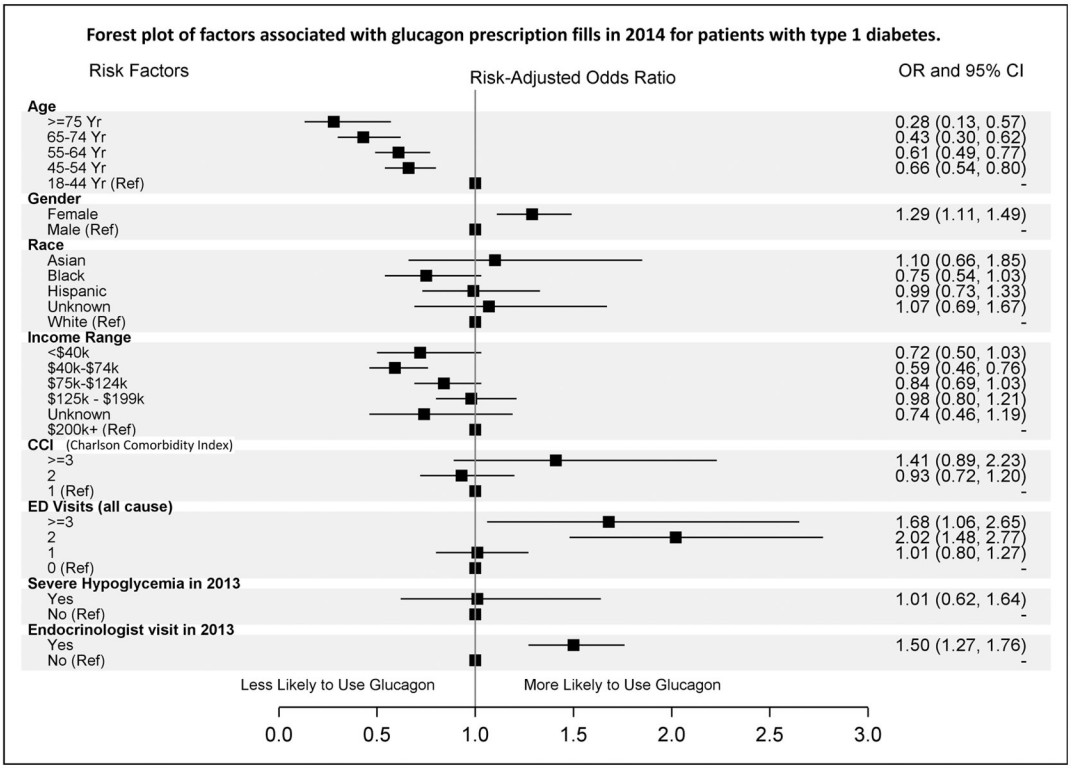
A



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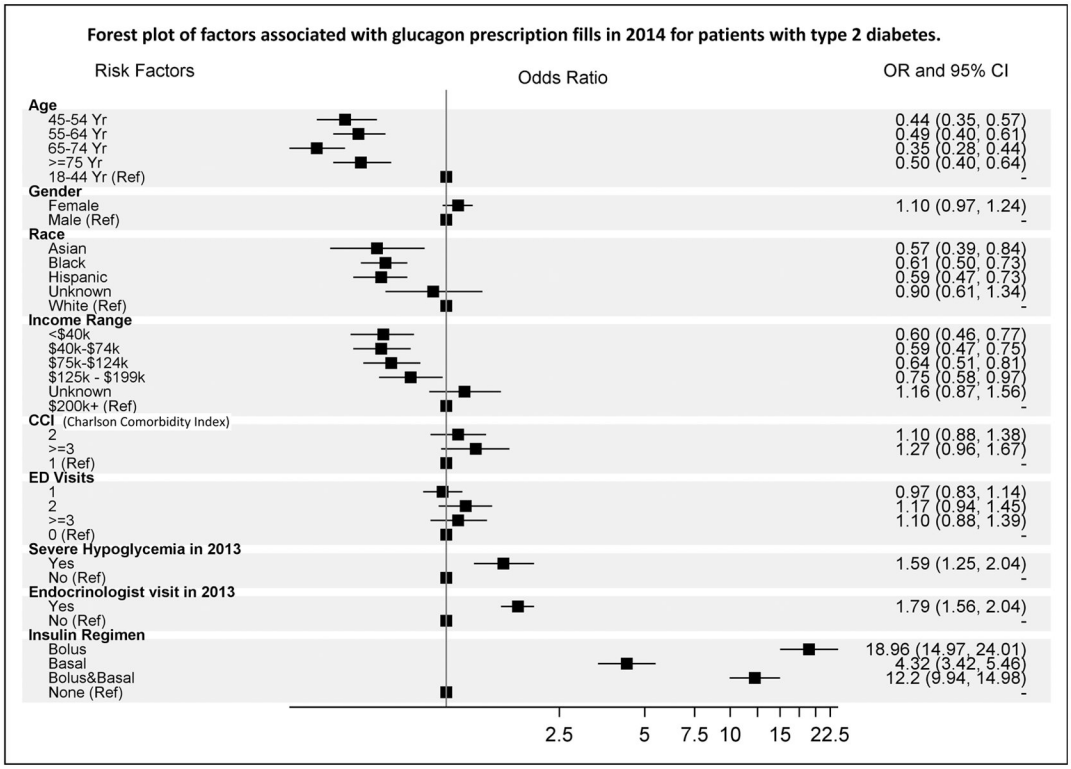

Fig. 1.

Forest plot of factors associated with glucagon prescription fills in 2014 for patients with type 1 diabetes (A) and type 2 diabetes (B). Multivariable analyses were adjusted for age, race, sex, income, Charlson Comorbidity Index and its individual components, depression, dementia, stroke, and peripheral vascular disease, Diabetes Complications Severity Index, use of biguanides, sulfonylureas, thiazolidinediones, meglitinides, dipeptidyl peptidase-4 inhibitors, sodium glucose cotransporter-2 inhibitors, and glucagon like peptide-1 receptor agonists, type of insulin regimen (basal, bolus, vs. basal and bolus; human vs. analog), all-cause Emergency Department (ED) visits, all-cause hospital admissions, severe hypoglycemia requiring ED visit or hospitalization in 2013, and endocrinology visits.

Table 1

Characteristics of patients with type 1 and type 2 diabetes who did and did not fill glucagon prescriptions in 2014.

	Patients with Type 1 Diabetes				Patients with Type 2 Diabetes			
	All Patients	**Patients with Glucagon Fills**	**Patients without Glucagon Fills**	**P-value**	**All Patients**	**Patients with Glucagon Fills**	**Patients without Glucagon Fills**	**P-value**
	N = 12338	**N = 1787**	**N = 10551**		**N = 323244**	**N = 2273**	**N = 320971**	
Age, years, %				<.001				<.001
18–44	6176 (50.1%)	1109 (62.1%)	5067 (48.0%)		22270 (6.9%)	288 (12.7%)	21982 (6.8%)	
45–54	2563 (20.8%)	305 (17.1%)	2258 (21.4%)		50112 (15.5%)	293 (12.9%)	49819 (15.5%)	
55–64	2089 (16.9%)	253 (14.2%)	1836 (17.4%)		81892 (25.3%)	534 (23.5%)	81358 (25.3%)	
65–74	1097 (8.9%)	91 (5.1%)	1006 (9.5%)		99599 (30.8%)	496 (21.8%)	99103 (30.9%)	
≥ 75	413 (3.3%)	29 (1.6%)	384 (3.6%)		69371 (21.5%)	662 (29.1%)	68709 (21.4%)	
Sex, Female %	5593 (45.3%)	913 (51.1%)	4680 (44.4%)	<.001	155101 (48.0%)	1242 (54.6%)	153859 (47.9%)	<.001
Race, %				0.012				<.001
Asian	221 (1.8%)	29 (1.6%)	192 (1.8%)		15149 (4.7%)	45 (2.0%)	15104 (4.7%)	
Black	895 (7.3%)	103 (5.8%)	792 (7.5%)		48677 (15.1%)	275 (12.1%)	48402 (15.1%)	
Hispanic	811 (6.6%)	98 (5.5%)	713 (6.8%)		38430 (11.9%)	184 (8.1%)	38246 (11.9%)	
White	10112 (82.0%)	1516 (84.8%)	8596 (81.5%)		213745 (66.1%)	1724 (75.8%)	212021 (66.1%)	
Unknown	299 (2.4%)	41 (2.3%)	258 (2.4%)		7243 (2.2%)	45 (2.0%)	7198 (2.2%)	
Household Income, %				<.001				<.001
<$40k	764 (6.2%)	76 (4.3%)	688 (6.5%)		61718 (19.1%)	414 (18.2%)	61304 (19.1%)	
$40k–$74k	2191 (17.8%)	245 (13.7%)	1946 (18.4%)		95205 (29.5%)	567 (24.9%)	94638 (29.5%)	
$75k–$124k	3816 (30.9%)	552 (30.9%)	3264 (30.9%)		91251 (28.2%)	564 (24.8%)	90687 (28.3%)	
$125k – $199k	2751 (22.3%)	450 (25.2%)	2301 (21.8%)		40390 (12.5%)	275 (12.1%)	40115 (12.5%)	
$200k+	2439 (19.8%)	409 (22.9%)	2030 (19.2%)		22170 (6.9%)	183 (8.1%)	21987 (6.9%)	
Unknown	377 (3.1%)	55 (3.1%)	322 (3.1%)		12510 (3.9%)	270 (11.9%)	12240 (3.8%)	
Charlson Comorbidity Index, %			0.087				<.001	
0 to 1	6788 (55.0%)	1023 (57.2%)	5765 (54.6%)		129868 (40.2%)	422 (18.6%)	129446 (40.3%)	
2	3498 (28.4%)	471 (26.4%)	3027 (28.7%)		87302 (27.0%)	469 (20.6%)	86833 (27.1%)	
≥ 3	2052 (16.6%)	293 (16.4%)	1759 (16.7%)		106074 (32.8%)	1382 (60.8%)	104692 (32.6%)	
Insulin	12338 (100%)	1787 (100%)	10551 (100%)	>.999	91477 (28.3%)	2022 (89.0%)	89455 (27.9%)	<.001

Insulin Regimen, %				<.001			<.001
Bolus	5799 (47.0%)	977 (54.7%)	4822 (45.7%)		8347 (2.6%)	440 (19.4%)	7907 (2.5%)
Basal	1040 (8.4%)	51 (2.9%)	989 (9.4%)		38706 (12.0%)	318 (14.0%)	38388 (12.0%)
Bolus & Basal	5461 (44.3%)	758 (42.4%)	4703 (44.6%)		42313 (13.1%)	1237 (54.4%)	41076 (12.8%)
Baseline HbA1c Level (Sub-sample)	**N = 3653**	**N = 466**	**N = 3187**		**N = 111237**	**N = 591**	**N = 110646**
Baseline HbA1c, %				0.761			<.001
<6%	123 (3.4%)	17 (3.6%)	106 (3.3%)		10117 (9.1%)	26 (4.4%)	10091 (9.1%)
6-<7%	743 (20.3%)	102 (21.9%)	641 (20.1%)		42260 (38.0%)	124 (21.0%)	42136 (38.1%)
7-<8%	1160 (31.8%)	148 (31.8%)	1012 (31.8%)		28048 (25.2%)	168 (28.4%)	27880 (25.2%)
8-<9%	796 (21.8%)	103 (22.1%)	693 (21.7%)		13356 (12.0%)	126 (21.3%)	13230 (12.0%)
≥9%	831 (22.7%)	96 (20.6%)	735 (23.1%)		17456 (15.7%)	147 (24.9%)	17309 (15.6%)
All Cause Emergency Department Visits and Hospitalizations, %				<.001			<.001
0	9575 (77.6%)	1299 (72.7%)	8276 (78.4%)		223048 (69.0%)	1159 (51.0%)	221889 (69.1%)
1	1582 (12.8%)	256 (14.3%)	1326 (12.6%)		52868 (16.4%)	447 (19.7%)	52421 (16.3%)
2	652 (5.3%)	130 (7.3%)	522 (4.9%)		23163 (7.2%)	244 (10.7%)	22919 (7.1%)
≥3	529 (4.3%)	102 (5.7%)	427 (4.0%)		24165 (7.5%)	423 (18.6%)	23742 (7.4%)
Endocrinologist visit in 2013	7601 (61.6%)	1290 (72.2%)	6311 (59.8%)	<.001	39736 (12.3%)	779 (34.3%)	38957 (12.1%)	<.001
Prior Severe Hypoglycemia in 2013, %	298 (2.4%)	62 (3.5%)	236 (2.2%)	0.002	4866 (1.5%)	185 (8.1%)	4681 (1.5%)	<.001