

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** American Community Survey Census Indicators

Shown are the survey census indicators, table references, and factor score coefficients from 2012-2017 that were used for area deprivation index (ADI) derivation.

U.S. Census Indicator	2012-2017 ACS Table Reference, 5-yr estimates	Factor Score Coefficients	
		2016	2017
Median family income	B19013	-0.16087	-0.16993
Income disparity	B19001	0.08019	0.06799
Families below poverty level	B17010	0.12555	0.12298
Percent population below 150% poverty threshold	C17002	0.22914	0.23659
Single parent household with dependents <18 years old	B23008	0.03817	0.04165
Households without a motor vehicle	B25044	0.05666	0.05646
Households without a telephone	B25043	0.00685	0.00892
Occupied housing units without complete plumbing	B25016	0.02692	0.02963
Owner occupied housing units	B25003	-0.00888	-0.00733
Households with >1 person per room	B25014	0.03546	0.03747
Median monthly mortgage	B25088	-0.13578	-0.13004
Median gross rent	B25064	-0.05922	-0.06295
Median home value	B25077	-0.07345	-0.0749
Employed persons ≥16 years old in white collar occupation	C24010	-0.02079	-0.01947
Civilian labor force unemployed (aged ≥16)	B23025	0.0228	0.02451
Population aged ≥25 years with <9-year education	B15003	0.00431	0.01132
Population aged ≥25 years with at least a high school education	B15003	-0.22112	-0.21015

**eTable 2.** Codes Used to Ascertain Hypoglycemia and DKA/HHS-Related Hospitalizations and Emergency Department Visits

Health condition	ICD-9 codes	ICD-10 codes
<b>Hypoglycemia</b>	251.0, 251.1, 251.2, 270.3, 962.3 or 250.8x (and not 259.8, 272.7, 681.xx, 682.xx, 686.9x, 707.1-707.9, 709.3, 730.0-730.2, 731.8) <i>per Ginde, et al(1)</i>	E08.641, E08.649, E09.641, E09.649, E10.641, E10.649, E11.641, E11.649, E13.641, E13.649, E15, E160, E161, E162, T383X1A, T383X1D, T383X1S, T383X2A, T383X2D, T383X2S, T383X3A, T383X3D, T383X3S, T383X4A, T383X4D, T383X4S, T383X5A, T383X5D, T383X5S
<b>DKA/HHS</b>	250.1x, 250.2x	E10.10, E10.11, E11.00, E11.01, E11.641, E13.10

Abbreviations: DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state.

**eTable 3.** Classification of Glucose-Lowering Medications

Combination medications were considered as separate agents belonging to each ingredient class.

Medication class	Included agents
<b>Biguanides</b>	Metformin
<b>Sulfonylureas</b>	Glimepiride Glipizide Glyburide
<b>Thiazolidinediones</b>	Pioglitazone Rosiglitazone
<b>DPP-4 inhibitors</b>	Alogliptin Linagliptin Sitagliptin Saxagliptin
<b>GLP-1 receptor analogs</b>	Exenatide Liraglutide Albiglutide Dulaglutide Semaglutide Lixisenatide
<b>SGLT2 inhibitors</b>	Canagliflozin Empagliflozin Dapagliflozin Ertugliflozin
<b>Glinides</b>	Nateglinide Repaglinide
<b>Amylin analogs</b>	Pramlintide
<b><math>\alpha</math>-Glucosidase inhibitors</b>	Acarbose Miglitol
<b>Basal insulin</b>	<u>Human</u> NPH Isophane  <u>Analog</u> Detemir Glargine Degludec
<b>Bolus insulin</b>	<u>Human</u> Regular  <u>Analog</u> Aspart Lispro Glulisine Inhaled powder insulin

**eTable 4.** Risk Factors of Severe Hypoglycemia and DKA/HHS (Sensitivity Analysis Using the Partially Adjusted Model)

Results of negative binomial regression analyses adjusted only for patient demographics (age, sex, health plan) and percent White residents in the county.

	<b>Hypoglycemia</b>		<b>DKA/HHS</b>	
	<b>IRR (95% CI)</b>	<b>p-value</b>	<b>IRR (95% CI)</b>	<b>p-value</b>
<b>Percent White residents in county</b>	0.64 (0.51-0.82)	<0.001	0.78 (0.62-0.99)	0.04
<b>ADI quintile</b>				
Q1 (least deprived)	Ref		Ref	
Q2	1.00 (0.91-1.09)	0.96	1.02 (0.92-1.12)	0.75
Q3	1.17 (1.06-1.28)	0.002	1.24 (1.11-1.37)	<0.001
Q4	1.15 (1.03-1.29)	0.02	1.12 (0.99-1.26)	0.07
Q5 (most deprived)	1.48 (1.33-1.64)	<0.001	1.11 (0.99-1.26)	0.08
<b>Sex</b>				
Female	Ref		Ref	
Male	0.93 (0.90-0.96)	<0.001	0.84 (0.79-0.88)	<0.001
<b>Health Plan</b>				
Commercial	Ref		Ref	
Medicare Advantage	4.82 (4.45-5.21)	<0.001	3.34 (3.05-3.65)	<0.001
<b>Age, years</b>				
18-44	Ref		Ref	
45-64	0.58 (0.53-0.64)	<0.001	0.17 (0.15-0.18)	<0.001
65-74	0.35 (0.32-0.39)	<0.001	0.04 (0.04-0.05)	<0.001
≥75	0.49 (0.44-0.54)	<0.001	0.04 (0.03-0.04)	<0.001

Abbreviations: ADI, area deprivation index; DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state.

**eTable 5.** Estimated Rates of Severe Hypoglycemia and DKA/HHS (Sensitivity Analysis Using the Partially Adjusted Model)

Rates of severe hypoglycemia and DKA/HHS per 1000 person-years, analyses adjusted only for patient demographics (age, sex, health plan) and percent White residents in the county.

	<b>Hypoglycemia</b> Rate per 1000 PY (95% CI)	<b>DKA/HHS</b> Rate per 1000 PY (95% CI)
<b>ADI quintile</b>		
Q1 (least deprived)	11.16 (10.60-11.73)	5.73 (5.38-6.09)
Q2	11.14 (10.22-12.05)	5.83 (5.34-6.32)
Q3	13.01 (11.91-14.10)	7.08 (6.45-7.71)
Q4	12.86 (11.53-14.19)	6.40 (5.73-7.07)
Q5 (most deprived)	16.49 (15.09-17.89)	6.39 (5.72-7.05)

Abbreviations: ADI, area deprivation index; DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state; PY, person-years.

**eTable 6.** Estimated Rates of Severe Hypoglycemia and DKA/HHS in Subgroups of Patient Age

Rates of severe hypoglycemia and DKA/HHS per 1000 person-years, analyses adjusted for patient demographics (age, sex, health plan), percent White residents in the county, comorbidities, and medications (fully adjusted model). \*p <0.05 for the IRR of the quintile examined (Q2-Q5) with ADI Q1 (least deprived) serving as the reference group.

	<b>Hypoglycemia</b>		<b>DKA/HHS</b>	
	<b>IRR (95% CI)</b>	<b>Rate per 1000 PY (95% CI)</b>	<b>IRR (95% CI)</b>	<b>Rate per 1000 PY (95% CI)</b>
<b>18-44 years old</b>				
Q1 (least deprived)	Ref	11.42 (9.45-13.39)	Ref	28.93 (25.28-32.57)
Q2	1.16 (0.97-1.38)	13.21 (10.75-15.66)	1.09 (0.92-1.29)	31.51 (26.80-36.21)
Q3	0.90 (0.73-1.10)	10.26 (8.16-12.37)	1.17 (0.99-1.39)	33.87 (28.98-38.75)
Q4	1.27 (1.03-1.57)*	14.54 (11.64-17.44)	1.31 (1.07-1.60)*	37.80 (30.97-44.64)
Q5 (most deprived)	1.24 (0.94-1.65)	14.22 (10.59-17.85)	1.42 (1.11-1.82)*	40.99 (31.26-50.72)
<b>45-64 years old</b>				
Q1 (least deprived)	Ref	11.61 (10.66-12.56)	Ref	7.75 (6.88-8.61)
Q2	0.96 (0.87-1.07)	11.17 (10.08-12.27)	1.04 (0.93-1.17)	8.08 (7.20-8.97)
Q3	1.05 (0.94-1.17)	12.16 (10.87-13.45)	1.15 (1.01-1.30)*	8.88 (7.76-9.99)
Q4	1.03 (0.91-1.17)	11.99 (10.54-13.44)	1.06 (0.92-1.21)	8.18 (7.14-9.21)
Q5 (most deprived)	1.29 (1.14-1.46)*	15.00 (13.24-16.76)	1.00 (0.84-1.19)	7.76 (6.47-9.05)
<b>65-74 years old</b>				
Q1 (least deprived)	Ref	13.42 (12.55-14.30)	Ref	4.11 (3.49-4.74)
Q2	0.97 (0.88-1.07)	13.03 (11.85-14.21)	0.94 (0.81-1.10)	3.88 (3.33-4.43)
Q3	1.14 (1.02-1.27)*	15.33 (13.90-16.75)	1.12 (0.95-1.33)	4.62 (3.91-5.32)
Q4	1.20 (1.05-1.37)*	16.05 (14.04-18.05)	1.14 (0.95-1.35)	4.67 (3.90-5.44)
Q5 (most deprived)	1.37 (1.22-1.54)*	18.44 (16.64-20.23)	1.10 (0.92-1.33)	4.53 (3.79-5.28)
<b>≥75 years old</b>				
Q1 (least deprived)	Ref	17.79 (16.71-18.87)	Ref	3.18 (2.83-3.53)
Q2	1.06 (0.96-1.16)	18.77 (17.19-20.35)	0.99 (0.86-1.15)	3.15 (2.73-3.58)
Q3	1.18 (1.07-1.31)*	21.05 (19.23-22.88)	1.09 (0.95-1.26)	3.47 (3.03-3.91)
Q4	1.17 (1.03-1.32)*	20.75 (18.47-23.03)	1.09 (0.91-1.31)	3.47 (2.86-4.08)
Q5 (most deprived)	1.55 (1.38-1.74)*	27.60 (24.82-30.39)	1.13 (0.95-1.35)	3.59 (3.01-4.17)

Abbreviations: ADI, area deprivation index; DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state; PY, person-years.

**eTable 7.** Estimated Rates of Severe Hypoglycemia and DKA/HHS in Subgroups of Patient Sex

Rates of severe hypoglycemia and DKA/HHS per 1000 person-years, analyses adjusted for patient demographics (age, sex, health plan), percent White residents in the county, comorbidities, and medications (fully adjusted model). \*p <0.05 for the IRR of the quintile examined (Q2-Q5) with ADI Q1 (least deprived) serving as the reference group.

	<b>Hypoglycemia</b>		<b>DKA/HHS</b>	
	<b>IRR (95% CI)</b>	<b>Rate per 1000 PY (95% CI)</b>	<b>IRR (95% CI)</b>	<b>Rate per 1000 PY (95% CI)</b>
<b>Men</b>				
Q1 (least deprived)	Ref	12.52 (11.88-13.15)	Ref	7.22 (6.42-8.01)
Q2	1.00 (0.93-1.08)	12.51 (11.64-13.37)	0.95 (0.85-1.07)	6.87 (6.06-7.68)
Q3	1.11 (1.01-1.22)*	13.89 (12.65-15.12)	1.08 (0.96-1.21)	7.80 (6.82-8.77)
Q4	1.11 (1.01-1.23)*	13.95 (12.66-15.25)	1.05 (0.93-1.20)	7.60 (6.66-8.55)
Q5 (most deprived)	1.32 (1.19-1.47)*	16.57 (14.98-18.16)	1.06 (0.91-1.23)	7.63 (6.55-8.72)
<b>Women</b>				
Q1 (least deprived)	Ref	14.54 (13.63-15.46)	Ref	7.75 (7.09-8.42)
Q2	1.01 (0.92-1.11)	14.74 (13.63-15.85)	1.09 (0.99-1.20)	8.46 (7.71-9.21)
Q3	1.13 (1.02-1.25)*	16.48 (15.03-17.93)	1.19 (1.07-1.32)*	9.20 (8.27-10.13)
Q4	1.18 (1.06-1.32)*	17.21 (15.45-18.96)	1.19 (1.06-1.35)*	9.25 (8.19-10.31)
Q5 (most deprived)	1.48 (1.34-1.63)*	21.51 (19.72-23.31)	1.17 (1.02-1.35)*	9.09 (7.86-10.31)

Abbreviations: ADI, area deprivation index; DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state; PY, person-years.



**eTable 8.** Estimated Rates of Severe Hypoglycemia and DKA/HHS in Subgroups of Glucose-Lowering Therapy

Rates of severe hypoglycemia and DKA/HHS per 1000 person-years, analyses adjusted for patient demographics (age, sex, health plan), percent White residents in the county, comorbidities, and medications (fully adjusted model). \*p <0.05 for the IRR of the quintile examined (Q2-Q5) with ADI Q1 (least deprived) serving as the reference group.

	Hypoglycemia		DKA/HHS	
	IRR (95% CI)	Rate per 1000 PY (95% CI)	IRR (95% CI)	Rate per 1000 PY (95% CI)
<b>Bolus ± basal insulin</b>				
Q1 (least deprived)	Ref	43.04 (40.79-45.29)	Ref	25.97 (23.87-28.07)
Q2	1.01 (0.94-1.10)	43.68 (40.69-46.66)	1.11 (0.99-1.24)	28.82 (26.02-31.62)
Q3	1.03 (0.95-1.12)	44.44 (41.27-47.62)	1.25 (1.13-1.39)*	32.52 (29.84-35.19)
Q4	1.10 (1.00-1.21)	47.19 (43.17-51.2)	1.16 (0.99-1.35)	30.11 (26.01-34.21)
Q5 (most deprived)	1.30 (1.18-1.43)*	55.79 (51.02-60.57)	1.16 (0.98-1.38)	30.20 (25.64-34.77)
<b>Basal insulin</b>				
Q1 (least deprived)	Ref	22.89 (21.26-24.52)	Ref	9.40 (8.17-10.64)
Q2	1.01 (0.91-1.12)	23.14 (21.39-24.89)	0.93 (0.78-1.13)	8.78 (7.35-10.21)
Q3	1.19 (1.06-1.33)*	27.14 (24.52-29.77)	1.04 (0.88-1.24)	9.81 (8.28-11.34)
Q4	1.18 (1.04-1.34)*	26.96 (24.06-29.86)	1.19 (0.99-1.42)	11.15 (9.43-12.87)
Q5 (most deprived)	1.33 (1.18-1.50)*	30.45 (27.33-33.57)	1.16 (0.94-1.44)	10.91 (8.76-13.07)
<b>Non-insulin drugs only</b>				
Q1 (least deprived)	Ref	5.44 (5.11-5.77)	Ref	1.67 (1.51-1.83)
Q2	1.03 (0.93-1.15)	5.63 (5.14-6.11)	0.99 (0.87-1.14)	1.66 (1.49-1.83)
Q3	1.11 (0.99-1.24)	6.03 (5.44-6.62)	1.07 (0.93-1.23)	1.79 (1.61-1.96)
Q4	1.13 (1.00-1.28)	6.15 (5.44-6.85)	1.07 (0.93-1.25)	1.79 (1.58-2.01)
Q5 (most deprived)	1.48 (1.32-1.65)*	8.03 (7.29-8.77)	1.01 (0.86-1.20)	1.69 (1.47-1.92)

Abbreviations: ADI, area deprivation index; DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state; PY, person-years.

**eTable 9.** Estimated Rates of Severe Hypoglycemia and DKA/HHS in Subgroups of Patient Health Plans

Rates of severe hypoglycemia and DKA/HHS per 1000 person-years, analyses adjusted for patient demographics (age, sex, health plan), percent White residents in the county, comorbidities, and medications (fully adjusted model). \*p <0.05 for the IRR of the quintile examined (Q2-Q5) with ADI Q1 (least deprived) serving as the reference group.

	Hypoglycemia		DKA/HHS	
	IRR (95% CI)	Rate per 1000 PY (95% CI)	IRR (95% CI)	Rate per 1000 PY (95% CI)
<b>Commercial insurance</b>				
Q1 (least deprived)	Ref	6.02 (5.51-6.52)	Ref	8.01 (7.31-8.72)
Q2	0.97 (0.86-1.10)	5.85 (5.18-6.53)	1.10 (0.98-1.25)	8.86 (7.84-9.87)
Q3	0.97 (0.86-1.11)	5.87 (5.12-6.61)	1.16 (1.05-1.30)*	9.33 (8.42-10.24)
Q4	0.99 (0.83-1.19)	5.98 (4.89-7.06)	1.15 (0.96-1.36)	9.18 (7.72-10.64)
Q5 (most deprived)	1.31 (1.10-1.56)*	7.89 (6.51-9.26)	1.25 (1.05-1.50)*	10.04 (8.33-11.74)
<b>Medicare Advantage</b>				
Q1 (least deprived)	Ref	17.73 (16.8-18.67)	Ref	7.02 (6.30-7.74)
Q2	1.02 (0.94-1.11)	18.03 (16.75-19.31)	0.96 (0.86-1.07)	6.72 (6.00-7.44)
Q3	1.16 (1.05-1.27)*	20.52 (18.87-22.17)	1.12 (1.00-1.24)	7.83 (6.95-8.70)
Q4	1.18 (1.07-1.31)*	20.99 (19.03-22.95)	1.11 (0.98-1.26)	7.80 (6.86-8.74)
Q5 (most deprived)	1.43 (1.30-1.57)*	25.3 (23.27-27.32)	1.07 (0.93-1.22)	7.49 (6.53-8.46)

Abbreviations: ADI, area deprivation index; DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state; PY, person-years.

## **eReference**

1. Ginde AA, Blanc PG, Lieberman RM, Camargo CA, Jr. Validation of ICD-9-CM coding algorithm for improved identification of hypoglycemia visits. *BMC Endocr Disord* 2008;8:4