Trends and Factors Associated With Very High Glycemia and Noninitiation of Insulin Therapy in U.S. Adults With Type 2 Diabetes, 1999–2018

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The prevalence of type 2 diabetes (T2D) has almost doubled since 1980 with targeted glycated hemoglobin (A1C) <7% being recommended to prevent complications (1). A recent study reported that 41% of a cohort of 35,304 patients with T2D from the U.S. and Sweden had suboptimal glycemic control (2). Therapeutic inertia, defined as "the failure to advance or deintensify treatment" when appropriate to do so (3), is a key driver of uncontrolled hyperglycemia. The current evidence-based clinical guidelines (1) recommend early initiation of insulin in cases of very high glycemia (VHG) (i.e., A1C >10% or blood glucose levels ≥300 mg/dL [16.7 mmol/L]). Although therapeutic inertia can occur at any time during the disease process, it is more likely at insulin initiation due to fear of hypoglycemia or weight gain (3). Epidemiological data on therapeutic inertia to insulin initiation are limited, and factors associated with noninitiation of insulin treatment despite VHG (NIIT) remain unexplored at the population level.

In U.S. adults with T2D, we aimed to identify factors associated with both VHG and NIIT and to report the trends from 1999 to 2018.

The National Health and Nutrition Examination Survey (NHANES) surveys were approved by the National Center for Health Statistics Research Ethics Review Board (4), and all participants provided written informed consent.

We included nonpregnant individuals aged ≥20 years with known diabetes and pooled NHANES waves into five time intervals (1999–2002, 2003–2006, 2007–2010, 2011–2014, and 2015–2018) to improve the precision of our estimates. We used binomial regression to estimate the age-adjusted prevalence for both outcomes, and prevalence ratios across NHANES waves. To identify factors associated to outcomes, we estimated adjusted odds ratio (aORs) and 95% CI using multiple logistic regression. All statistical tests were two-sided, with a type I error probability of 5%.

Table 1 shows sex-stratified characteristics of 8,816 adults with diabetes and factors associated with outcomes. Non-Hispanic Caucasian individuals represented 39% of the population, 49.7% were aged ≥60 years, and 22.5% had an income-to-poverty ratio ≤1. In both sexes, non-Caucasian ethnicity was associated with higher odds ratio of both VHG and NIIT specifically in non-Hispanic African/African American (24.3%) and Hispanic female (13.3%) individuals. Hispanic male individuals had higher odds of VHG (aOR 5.11, 95% CI 2.17–12.01) with a trend toward higher odds of NITT (aOR 2.26, 95% CI, 0.99–5.17). Higher odds of both VHG and NIIT were also found in normotensive female patients (37.2%), patients with BMI ≥30 (33.9%), and male patients aged 20–40 years (6.6%). Poverty was associated with higher odds of VHG but not NIIT in both male (aOR 2.40, 95% CI 1.10–5.26) and female (aOR 2.85, 95% CI 1.04–7.80) individuals. Marital status, education level, and acculturation score were not associated with VHG or NIIT. In addition, smoking and chronic kidney disease did not increase the risk of VHG or NIIT.

Across the five NHANES waves, the overall prevalence of VHG dropped from 9.9% (1999–2002) to 5.6% (2015–2018), with a decrease in the age-adjusted prevalence for both VHG (17% to 10%) and NIIT (13% to 4%). In both sexes, accounting for the increasing prevalence of T2D, there was a significant linear trend of decreasing age-adjusted prevalence of NIIT from 1999–2002 (71 patients; 8.6%, 95% CI 6.8–10.8) to 2015–2018 (105 patients; 2.2%, 95% CI 1.8–2.6). After adjusting for age, sex, and race, we found that mean A1C decreased over time in participants who initiated insulin therapy (*P* for trend < 0.01) but not in those who never used insulin.

Among U.S. adults with T2D, *1*) the age-adjusted prevalence of both VHG and NIIT significantly decreased from 1999–2002 to 2015–2018; *2*) non-Caucasian ethnicity (i.e., being Black or Latino) is a major determinant of both VHG and NIIT,

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Table 1—Factors associated with VHG* and noninitiation of insulin treatment† in U.S. patients with T2D

	Male				Female			
	No. of participants	N1/N2‡	Model 1	Model 2‖	No. of participants	N1/N2‡	Model 1	Model 2‖
Age at interview, years								
20–40	244	50/30	1	1	310	41/17	1	1
40–59	1,715	146/105	**0.24 (0.13–0.45)**	**0.32 (0.18–0.57)**	1,597	150/91	0.97 (0.40–2.35)	1.18 (0.51–2.72)
≥60	2,419	82/34	**0.07 (0.03–0.16)**	**0.06 (0.02–0.14)**	2,107	96/42	0.69 (0.25–1.91)	0.75(0.23–2.42)
Missing values	178				141			
Race/ethnicity								
Non-Hispanic Caucasian	1,803	57/41	1	1	1,357	49/11	1	1
Non-Hispanic Africans/African Americans	1,020	76/54	**2.60 (1.24–5.46)**	**2.12 (1.03–4.37)**	1,121	93/55	**2.67 (1.29–5.49)**	**5.77 (2.73–12.18)**
Hispanic	1,064	124/74	**5.11 (2.17–12.01)**	2.26 (0.99–5.17)	1,172	127/78	**2.56 (1.20–5.48)**	**5.18 (2.24–11.97)**
Other	669	34/11	2.02 (0.38–10.69)	0.32 (0.08–1.21)	505	31/16	1.24 (0.34–4.50)	1.12 (0.22–5.68)
Education level								
Less than high school	1,444	115/74	1	1	1,463	138/74	1	1
High school	1,036	79/36	1.00 (0.54–1.84)	0.57 (0.30–1.08)	1,051	68/41	1.26 (0.62–2.55)	1.23 (0.59–2.59)
Some college or more	2,071	97/79	0.87 (0.48–1.62)	0.96 (0.53–1.76)	1,637	94/45	1.17 (0.67–2.05)	0.64 (0.35–1.16)
Missing values	5				4			
BMI, kg/m^2								
<25	558	51/41	1	1	414	41/20	1	1
25–29	1,454	116/79	0.94 (0.36–2.48)	0.59 (0.28–1.24)	929	90/54	0.82 (0.39–1.70)	0.86 (0.37–1.98)
≥30	2,253	120/58	**0.36 (0.16–0.81)**	**0.18 (0.08–0.44)**	2,481	164/82	0.58 (0.26–1.29)	0.54 (0.23–1.23)
Missing values	291				331			
Marital status								
Married/partnered	3,230	205/123	1	1	1,947	119/85	1	1
Separated/widowed	988	67/40	0.63 (0.29–1.40)	0.82 (0.43–1.58)	1,846	137/54	1.06 (0.67–1.66)	0.74 (0.45–1.21)
Single	327	18/16	0.85 (0.51–1.40)	0.89 (0.41–1.91)	341	42/19	0.82 (0.37–1.78)	0.99 (0.45–2.19)
Missing values	11				21			
Acculturation score¶								
5	1,059	86/56	1	1	1,157	110/72	1	1
3–4	2,487	123/71	0.60 (0.36–1.02)	0.69 (0.37–1.28)	1,975	129/50	0.88 (0.51–1.50)	0.70 (0.42–1.20)
0–2	1,010	82/53	**0.46 (0.26–0.83)**	0.67 (0.35–1.28)	1,020	61/38	1.23 (0.61–2.49)	1.18 (0.49–2.84)
Missing values					3			
Income-to-poverty ratio								
>4	995	37/30	1	1	585	21/16	1	1
2–4	2,391	154/91	1.44 (0.83–2.50)	1.28 (0.69–2.39)	2,098	108/73	1.30 (0.60–2.84)	0.95 (0.35–2.54)
≤1	719	81/51	**2.40 (1.10–5.26)**	2.06 (0.95–4.46)	919	125/47	**2.85 (1.04–7.80)**	1.30 (0.45–3.78)
Missing values	451				553			
Tobacco smoking								
No	3,589	196/126	1	1	3,545	255/137	1	1
Yes	967	95/54	1.20 (0.58–2.48)	0.80 (0.47–1.38)	610	45/23	1.38 (0.69–2.80)	1.26 (0.56–2.83)
Hypertension#								
No	807	8,457	1	1	663	94/55	1	1

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Table 1—Continued

	Male				Female			
	No. of participants	N1/N2‡	Model 1	Model 2‖	No. of participants	N1/N2‡	Model 1	Model 2‖
Yes	3,385	188/116	0.63 (0.35–1.12)	0.64 (0.36–1.13)	2,943	179/101	**0.45 (0.24–0.82)**	**0.50 (0.26–0.96)**
Missing values	364				549			
CKD**								
No	2,720	150/112	1	1	2,711	165/117	1	1
Yes	1,836	141/68	1.51 (1.00–2.30)	0.96 (0.53–1.72)	1,444	135/43	1.41 (0.87–2.28)	0.87 (0.49–1.56)
Taking insulin								
No	3,536	180	1	NA	3,236	160	1	NA
Yes	1,016	111	**2.36 (1.38–4.05)**	NA	916	140	**3.28 (2.00–5.38)**	NA
Missing values	4				3			

Data are *n* or adjusted odds ratio (95% CI). *Defined as being A1C >10% [86 mmol/mol] or blood glucose levels ≥300 mg/dL [16.7 mmol/L]. †Absence of insulin therapy despite very high glycemia. ‡N1, number of patients with very high glycemia; N2, number of patients with very high glycemia without insulin therapy. §Odds ratios for the association with very high glycemia. ‖Odds ratios for the association with noninitiation of insulin treatment despite very high glycemia. ¶Based on three proxy measures: country of birth, language spoken at home, and length of time in the U.S., ranging from 0 (least acculturated) to 5 (most acculturated). #Systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥90 mmHg. **Chronic kidney diseases defined as having reduced eGFR (<60 mL/min/1.73 m^2), albuminuria (≥30 mg/g), or both. Boldface type indicates statistically significant results ($P < 0.05$).

independent of education level; *3*) male but not female individuals diagnosed with T2D at young adulthood represent a high-risk group for both issues; and *4*) sex difference in the distribution of risk factors for both VHG and NIIT is evident. Poverty was associated with high odds of VHG but not with NIIT. Recent findings suggest that use of high-cost antidiabetes drugs in U.S. adults was determined by insurance status rather than by income (5). The distribution of insured versus uninsured patients across strata of income-to-poverty ratio may explain the null association between poverty and NIIT. A complete drug profile could not be established based on the NHANES data, so we could not account for treatments used by those who did not initiate insulin. The temporal changes in age-adjusted prevalences are partly due to current clinical guidelines and in keeping with previous studies (3). Targeted interventions accounting for those findings and emphasizing shared decision-making may help address NIIT in patients with T2D.

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