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Underrepresentation of Diverse Populations and Glycemic Outcomes in Major Clinical Trials of Automated Insulin Delivery[1]

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Dear Editor,

Individuals with type 1 diabetes (T1D) of minoritized racial/ethnic groups and low socioeconomic status (SES) access and use advanced diabetes technology at lower rates compared to non-Hispanic White (NHW) and high SES populations, [1] which has been associated with worse glycemic outcomes.[2] In addition to lower technology use, individuals of minoritized racial/ethnic groups, especially non-Hispanic Black and Hispanic groups, are vastly underrepresented in diabetes technology clinical trials. Our research center, which has conducted multiple major clinical trials of automated insulin delivery (AID) technology[3,4] recently performed a self-assessment study to determine the extent of underrepresentation of diverse populations in our studies and to compare differences in glycemic outcomes across race/ethnicity, education, and income.

The study included adult (> 21 years) data from four major AID trials (n=292) which collected household income (without information on household size) and education using $25k brackets and categories, respectively. Within this limitation, and given the skewed distribution of participants' income and education levels, we defined annual household income as "higher" if ≥$50,000 (average household income in Charlottesville, VA) and education as "higher" if greater than/equal to a bachelor's degree – these groups representing approximately 62% and 33% of the U.S. population, respectively.[5] Representation and glycemic outcomes of minoritized racial-ethnic groups were compared to those of NHW participants. Glycemic outcomes included HbA1c, time-in-range (TIR - 70 to 180 mg/dL), time-below-range (TBR - <70 mg/dL), and time-above-range (TAR - >180 mg/dL). Linear mixed regression models compared glycemic outcomes for variables distributed normally while adjusting for age, study, previous CGM and pump use and corresponding baseline outcomes. We reported mean±SD and median with interquartile ranges for normal distributions and skewed distributions, respectively.

Paralleling current literature, our trials overrepresented the NHW (83%), higher-income (91%), and higher-educated (86%) populations (Table 1). The percentages of minoritized racial/ethnic identities included in the study participants were 6% Hispanic, 3% Asian, 2% Black, and 6% multi-racial. Comparing baseline and final glycemic outcomes for NHW *versus* all minoritized racial/ethnic groups, there were no significant differences (Table 1A). For education, there were differences in baseline HbA1c in those with low compared to

those with high (p<0.001) education levels, as well as for TIR (p<0.001) and TAR (p<0.001). Post-AID, these differences disappeared for HbA1c (p=0.113), marginally improved for TIR (p=0.054) but did not improve significantly for TBR and TAR (Table 1B). For income, baseline TBR was higher for participants with low *versus* high incomes (p=0.028). However, this difference resolved after AID use (Table 1C).

Failure to find differences between race/ethnicity groups in baseline and post-AID glycemic metrics may have been due to the small sample size and higher income/education levels of our minoritized racial/ethnic participants. Possibly due to this small and skewed sample of racial/ethnic minority groups, baseline and post-trial glycemic status were more highly associated with income and education than race/ethnicity. However, we recognize that our analysis could not sufficiently address systemic racism, provider bias, and medical mistrust, which contribute to underrepresentation and worse glycemic outcomes among minoritized racial/ethnic groups.[6] Moreover, baseline glycemic differences associated with level of education were not completely eradicated with AID use. Despite these limitations, this self-assessment clearly identified underrepresentation and glycemic disparities in clinical trials at our research center.

This was highly beneficial, resulting in the implementation of strategies to increase the diversity in our clinical trial population, which included outreach to more diverse groups through purposive sampling approaches, community outreach events, and collaboration with public health leadership. We also are making strides to remove potential financial barriers to study participation via increased transportation/study-related funding. We encourage other diabetes research groups to conduct similar self-assessments which can lead to implementation of strategies to begin to rectify the problem of underrepresentation In addition, our findings suggest that improving accessibility to AID may help to equalize disparities in glycemic outcome associated with SES factors such as income, and that it is important for clinical trials to include participants who represent, not only racial/ethnic diversity, but also underrepresented SES backgrounds.

Author Disclosure Statement

J.G-T. reports receiving industry research support and royalties from Dexcom through his institution. No other competing financial interests exist for the remaining authors.

Authors' Contributions

J.G-T. was involved in verifying and analyzing the data and writing and editing the article. O.V. was involved in verifying and analyzing the data, performing the statistical analyses, and writing and editing the article. M.H. was involved in verifying and analyzing the data and writing and editing the article. A.B. was involved in verifying and analyzing the data and writing and editing the article. L.F-G. was involved in verifying and analyzing the data and writing and editing the article.

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Table 1. Baseline and final glycemic metrics for race/ethnicity, education, and income groups.

A.	**Minoritized Racial/Ethnic participants (MRE)**				**Non-Hispanic White participants (NHW)**				**Baseline**		**Final**	
	Baseline	Final	Mean adjusted treatment difference (Baseline-Final), [95%CI]	*p*-value	Baseline	Final	Mean adjusted treatment difference (Baseline-Final), [95%CI]	*p*-value	Mean adjusted treatment difference (MRE - NHW), [95%CI]	*p*-value	Mean adjusted treatment difference (MRE - NHW), [95%CI]	*p*-value
N	49	49			240	239						
HbA1c (%)	7.56 ± 0.15	7.26 ± 0.15	-0.30 [-0.55 to -0.04]	0.022	7.37 ± 0.07	7.06 ± 0.07	-0.31 [-0.43 to -0.20]	<.001	0.19 [-0.13 to 0.50]	0.246	0.20 [-0.12 to 0.52]	0.218
TIR 70-180 (%)	56.77 ± 2.47	67.26 ± 2.47	10.49 [6.96 to 14.02]	<.001	59.45 ± 1.11	69.33 ± 1.13	9.88 [8.23 to 11.53]	<.001	-2.68 [-8.00 to 2.65]	0.324	-2.07 [-7.42 to 3.28]	0.447
TBR 70	3.92 ± 0.50	1.99 ± 0.50	-1.94 [-2.86 to -1.02]	<.001	3.93 ± 0.22	1.76 ± 0.23	-2.16 [-2.59 to -1.73]	<.001	0.00 [-1.08 to 1.07]	0.996	0.22 [-0.86 to 1.31]	0.688
TAR 180	39.29 ± 2.61	30.77 ± 2.61	-8.51 [-12.24 to -4.79]	<.001	36.64 ± 1.17	28.91 ± 1.20	-7.73 [-9.47 to -5.99]	<.001	2.64 [-2.97 to 8.25]	0.355	1.86 [-3.77 to 7.49]	0.517

B.

	< Bachelor's degree participants				≥ Bachelor's degree participants				Baseline		Final	
	Baseline	Final	Mean adjusted treatment difference (Baseline-Final), [95%CI]	*p*-value	Baseline	Final	Mean adjusted treatment difference (Baseline-Final), [95%CI]	*p*-value	Mean adjusted treatment difference (<Bachelor - ≥ Bachelor), [95%CI]	*p*-value	Mean adjusted treatment difference (< Bachelor - ≥ Bachelor), [95%CI]	*p*-value
N	34	34			208	208						
HbA1c (%)	7.83 ± 0.16	7.29 ± 0.16	-0.54 [-0.76 to -0.31]	<.001	7.25 ± 0.07	7.02 ± 0.07	-0.23 [-0.33 to -0.13]	<.001	0.58 [0.25 to 0.92]	<.001	0.27 [-0.07 to 0.61]	0.113
TIR 70-180 (%)	50.07 ± 2.75	64.37 ± 2.75	14.30 [10.22 to 18.37]	<.001	61.18 ± 1.22	70.18 ± 1.22	9.00 [7.19 to 10.81]	<.001	-11.10 [-17.01 to -5.19]	<.001	-5.81 [-11.72 to 0.11]	0.054
TBR 70	3.70 ± 0.61	1.78 ± 0.61	-1.92 [-3.02 to -0.82]	<.001	4.31 ± 0.27	1.92 ± 0.27	-2.39 [-2.88 to -1.91]	<.001	-0.61 [-1.92 to 0.70]	0.358	-0.14 [-1.45 to 1.17]	0.836
TAR 180	46.19 ± 2.91	33.74 ± 2.91	-12.44 [-16.75 to -8.14]	<.001	34.49 ± 1.29	27.91 ± 1.29	-6.58 [-8.50 to -4.67]	<.001	11.70 [5.43 to 17.96]	<.001	5.84 [-0.43 to 12.10]	0.068

Diabetes Technology and Therapeutics
of Diverse Populations and Glycemic Outcomes in Major Clinical Trials of Automated Insulin Delivery (DOI: 10.1089/dia.2023.0197)

C.

	Low-income participants (<$50k)				High-income participants (≥$50k)				Baseline		Final	
	Baseline	Final	Mean adjusted treatment difference (Baseline-Final), [95%CI]	*p*-value	Baseline	Final	Mean adjusted treatment difference (Baseline-Final), [95%CI]	*p*-value	Mean adjusted treatment difference (<$50k - ≥$50k), [95%CI]	*p*-value	Mean adjusted treatment difference (<$50k - ≥$50k), [95%CI]	*p*-value
N	19	19			184	184						
HbA1c (%)	7.53 ± 0.20	7.03 ± 0.20	-0.49 [-0.78 to -0.21]	<.001	7.33 ± 0.08	7.06 ± 0.08	-0.27 [-0.38 to -0.16]	<.001	0.19 [-0.23 to 0.61]	0.366	-0.03 [-0.45 to 0.39]	0.892
TIR 70-180 (%)	57.38 ± 3.69	66.00 ± 3.69	8.63 [3.41 to 13.84]	0.001	58.86 ± 1.39	69.38 ± 1.39	10.52 [8.56 to 12.49]	<.001	-1.48 [-9.24 to 6.27]	0.707	-3.38 [-11.13 to 4.37]	0.391
TBR 70	5.42 ± 0.74	1.86 ± 0.74	-3.56 [-4.89 to -2.23]	<.001	3.68 ± 0.28	1.87 ± 0.28	-1.81 [-2.31 to -1.31]	<.001	1.74 [0.19 to 3.29]	0.028	-0.01 [-1.56 to 1.54]	0.993
TAR 180	37.19 ± 3.87	32.00 ± 3.87	-5.19 [-10.68 to 0.30]	0.064	37.46 ± 1.46	28.76 ± 1.46	-8.70 [-10.76 to -6.63]	<.001	-0.27 [-8.41 to 7.86]	0.947	3.24 [-4.90 to 11.37]	0.434

TIR 70-180 means percentage of time-in-range 70 to 180 mg/dl, TBR percentage of time-below-range (less than 70 mg/dl) and TAR percentage of time-above-range (greater than 180 mg/dl).