Hybrid Closed-Loop Systems and Glycemic Outcomes in Children and Adults With Type 1 Diabetes: Real-World Evidence From a U.S.-Based Multicenter Collaborative

Nudrat Noor,[1,2a] Manmohan K. Kamboj,[3] Taylor Triolo,[4] Sarit Polsky,[4] Ryan J. McDonough,[5] Carla Demeterco-Berggren,[6] Laura Jacobsen,[7] Rona Sonabend,[8] Osagie Ebekozien,[1,9] and Daniel J. DeSalvo[8]

Diabetes Care 2022;45:e118–e119 | https://doi.org/10.2337/dc22-0329

Increasing evidence demonstrates the benefits of new diabetes technologies, including insulin pumps and continuous glucose monitors (CGM), for glycemic management in people with type 1 diabetes (T1D). In addition to the independent use of these technologies, hybrid closed-loop systems (HCLS), which combine insulin pumps and CGM with a closed-loop algorithm controller to automate insulin delivery, can improve glucose levels (1,2). This study compared glycemic outcomes in users of HCLS with those of users of insulin pumps and CGM without automated insulin delivery and those using multiple daily insulin injections (MDI) with CGM in youth and adults with T1D.

We analyzed electronic medical records data (2019–2021) from the T1D Exchange Quality Improvement Collaborative (T1DX-QIC), a multicenter database for people with T1D (3). A total of 28,019 people, aged ≥6 years with T1D diagnosis for at least 1 year, were classified into three groups by mode of insulin treatment and CGM use. At their most recent visit, patients who reported using HCLS (either Tandem t:slim X2 pump with Control-IQ or Medtronic 670G or 770G pump with active automated mode) were classified as HCLS users ($N = 2,047$), those using an insulin pump together with a CGM without automated insulin delivery were classified as Pump+CGM users ($N = 12,306$), and those using MDI for insulin therapy along with a CGM device were classified as MDI+CGM users ($N = 13,613$). DIY loopers (patients having built their own closed-loop systems) were excluded from this analysis. Primary outcome was the most recently recorded HbA_{1c} (in percent). Secondary outcomes, available for a subgroup of this population, included time in range (TIR), defined as percentage of time spent between 70 and 180 mg/dL, time below range (TBR) (<70 mg/dL), and time above range (TAR) (>250 mg/dL), using an average of the last 14 days. Data collection for this analysis was approved by the Western Institutional Review Board.

In this study, 58% of the HCLS group, 60% of the Pump+CGM group, and 59% of the MDI+CGM group were individuals ≤18 years of age. Inequities in HCLS use by race/ethnicity and insurance status were observed. Among all non-Hispanic (NH) Black people with T1D, 3% used HCLS, whereas in the NH White population, 8% used HCLS ($P < 0.001$). Differences in HCLS uptake persisted by race/ethnicity after stratifying by insurance status. Duration of diabetes was longer in the HCLS group than in the Pump+CGM and MDI+CGM groups (mean [SD] 11 [11] vs. 9 [9] and 9 [10] years). In assessment of glycemic outcomes, mean HbA_{1c} levels were lower for HCLS users than for the Pump+CGM group (difference in means [95% CI] −0.5 [−0.6, −0.5]) and the MDI+CGM group (difference in means [95% CI] −0.8 [−0.9, −0.7]; $P < 0.001$). HbA_{1c} levels were lowest in the HCLS group for both pediatric (aged ≤18 years) and adult (aged >18 years) populations (pediatric median HbA_{1c} [interquartile range] 7.5 [1.6] vs. 8.0 [2.0] and 8.2 [2.4], respectively; adult median HbA_{1c} [interquartile range] 7.0 [1.2] vs. 7.6 [1.8] and 7.7 [2.1], respectively). Linear mixed models, controlling for potential confounding effects of age, sex, race/ethnicity, and insurance status, showed that estimated marginal means (EMM) for HbA_{1c} remained lower among HCLS users than for the

[1]T1D Exchange, Boston, MA
[2]Aga Khan University, Karachi, Pakistan
[3]Nationwide Children's Hospital, Columbus, OH
[4]Barbara Davis Center for Diabetes, Aurora, CO
[5]Children's Mercy Kansas City, Kansas City, MO
[6]Rady Children's Hospital, San Diego, CA
[7]University of Florida, Florida, Gainesville, FL
[8]Texas Children's Hospital, Houston, TX
[9]University of Mississippi, Oxford, MS

Corresponding author: Nudrat Noor, nnoor@t1dexchange.org

Received 23 February 2022 and accepted 25 April 2022

O.E. and D.J.D. are co-senior authors.

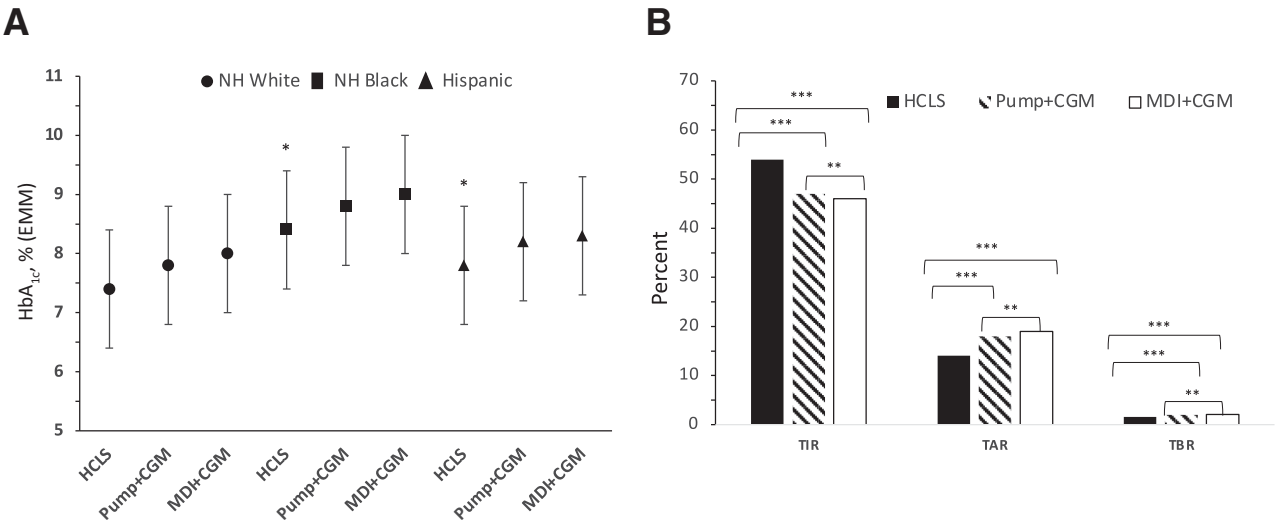

Figure 1–*A*: EMM for HbA_{1c} levels across insulin therapy use groups by race/ethnicity, adjusted for age, sex, and insurance type. *$P < 0.001$ (Bonferroni corrected) for comparison of HbA_{1c} in NH Black vs. NH White and Hispanic vs. NH White HCLS users by Mann-Whitney *U* test. *B*: EMM for TIR, TAR, and TBR, adjusted for age, sex, race/ethnicity, and insurance type. **$P < 0.01$; ***$P < 0.001$. *P* values were determined by Mann-Whitney *U* test and were Bonferroni corrected. The following numbers of samples were used: TIR, HCLS = 1,664 and insulin+pump = 7,629; time below 70 mg/dL, HCLS = 1,330 and insulin+pump = 10,484; time below 54 mg/dL, HCLS = 1,333 and insulin+pump = 10,484; time above 250 mg/dL, HCLS = 1,332 and insulin+pump = 10,416.

Pump+CGM and MDI+CGM comparator groups (EMM [95% CI] 8.1 [8.0, 8.2] vs. 8.7 [8.6, 8.8] and 8.8 [8.7, 8.9]; $P < 0.001$). Further, among all HCLS users, people of NH Black and Hispanic race/ethnicity had significantly higher adjusted HbA_{1c} levels than NH White peers (EMM [95% CI] 8.4 [7.4, 9.5] and 7.8 [6.8, 9.0] vs. 7.4 [6.4, 8.5]) (Fig. 1*A*).

Mean TIR was higher in the HCLS group than in the Pump+CGM and MDI+CGM groups (mean [SD] 60% [17] vs. 52% [20] and 50% [21], respectively; $P < 0.001$), TBR was lower in the HCLS group (mean [SD] 1.6% [1.4] vs. 2.0% [2.3] and 2.1% [2.3], respectively; $P < 0.001$), and TAR was also lower in the HCLS group (mean [SD] 14% [14] vs. 22% [17] and 21% [19], respectively; $P < 0.001$). Improved glycemic targets, including more TIR, less TBR, and less TAR, persisted for the HCLS group after adjustment for the abovementioned covariates for the overall population (Fig. 1*B*) as well as for the pediatric and adult populations separately.

This report demonstrates the value of HCLS use in lowering glycemic outcomes; however, a limitation of this cross-sectional study is that we were unable to rule out reverse causation, in that people with lower HbA_{1c} may be more likely to adopt HCLS. While the benefit of HCLS technology is apparent for both children and adults, the adult population showed better glycemic levels than the pediatric group, potentially owing to the inherent challenges in reaching optimal glycemic targets in children and young adults with T1D (4). Lastly, advanced diabetes technology use was lower in NH Black and publicly insured people, indicating that social disparities continue to be a hindrance to better health outcomes in this population (5). There remains a need to address inequities for vulnerable groups with diabetes.

Acknowledgments. The authors thank all team members and patients across all participating centers in the T1DX-QIC.

Funding. The T1DX-QIC is supported by the The Leona M. and Harry B. Helmsley Charitable Trust.

Duality of Interest. O.E. is a member of the Medtronic Diabetes Health Inequity Board. D.J.D. has served as an independent consultant for Dexcom and Insulet, and his institution has received research support from Insulet separate from this work.

Author Contributions. N.N. and O.E. conceptualized the study, N.N. wrote the draft manuscript and analyzed the data, and N.N., O.E., and D.J.D. contributed to the interpretation of data. All authors critically reviewed the manuscript and approved the final version. N.N. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Karges B, Schwandt A, Heidtmann B, et al. Association of insulin pump therapy vs insulin injection therapy with severe hypoglycemia, ketoacidosis, and glycemic control among children, adolescents, and young adults with type 1 diabetes. JAMA 2017;318:1358–1366

2. Brown SA, Kovatchev BP, Raghinaru D, et al.; iDCL Trial Research Group. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. N Engl J Med 2019; 381:1707–1717

3. Weinstock RS, Prahalad P, Rioles N, Ebekozien O. T1D Exchange Quality Improvement Collaborative: a learning health system to improve outcomes for all people with type 1 diabetes. Clin Diabetes 2021;39:251–255

4. Nathan DM, Genuth S, Lachin J, et al.; Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977–986

5. Majidi S, Ebekozien O, Noor N, et al. Inequities in health outcomes in children and adults with type 1 diabetes: data from the T1D Exchange Quality Improvement Collaborative. Clin Diabetes 2021;39:278–283