ISPAD–Breakthrough T1D Research Fellowship
Progress Report

Project title: Use of Time in Tight Range (70–140 mg/dL) as Primary Glycemic Target in Children and Adolescents with Type 1 Diabetes Using AID Systems: A Randomized Trial with Stepwise Introduction of Therapeutic Targets

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1. Introduction

Time in Tight Range (TITR; 70–140 mg/dL) has emerged as a clinically relevant continuous glucose monitoring (CGM) metric offering a closer approximation to euglycemia compared to the conventionally used Time in Range (TIR; 70–180 mg/dL). In healthy individuals, glucose levels fall within this range approximately 96% of the time (1), and TITR ≥50% has been proposed as a meaningful clinical target, particularly for individuals using automated insulin delivery (AID) systems (2). Despite its growing adoption in research and clinical practice, the feasibility and real-world impact of using TITR as the primary therapeutic goal in a pediatric setting had not yet been tested in a randomized trial, and its psychological implications remained largely unexplored.

This fellowship project aims to address these gaps through a 12-month, open-label randomized controlled trial with a stepped intervention design, conducted at the Pediatric Diabetes Unit, AOU “G. Martino”, University of Messina. The trial will compare TITR-based versus TIR-based management as the primary treatment target in adolescents aged 11–18 years with type 1 diabetes (T1D) using AID systems, assessing both glycemic and psychosocial outcomes.

The present report covers the first six months of the fellowship (November 2025 – May 2026), during which I conducted the preparatory and regulatory activities necessary to initiate the study, and completed a closely related observational study whose findings serve as key preliminary data for the fellowship project.

2. Progress on the Fellowship Project

2.1 Ethics Committee Approval

A main goal achieved during this reporting period was the formal approval of the study protocol by the Local Ethics Committee of the University Hospital “G. Martino”, Messina. Approval was granted on 27 March 2026 (Protocol No. 116-25). This authorization covers all aspects of the study, including patient recruitment, data collection, psychological assessments, and CGM data management.

2.2 Study Preparation and Initiation of Recruitment

Following ethics approval, the preparatory phases for study initiation have begun. These included the training of the multidisciplinary team (pediatric endocrinologists, diabetes nurses, and psychologist) on study procedures and outcome measures. Participant recruitment has been initiated, with the identification and screening of the first eligible candidates among the established cohort of adolescents with T1D followed at our center who use AID systems.

2.3 Preliminary Study: Psychological Impact of TITR in Adolescents with T1D

A key output of this reporting period is the publication of a cross-sectional observational study directly related to the scientific rationale of the fellowship project. This work, conducted at the Pediatric Diabetes Unit of the University of Messina, represents the first quantitative assessment of the psychological impact of TITR in adolescents with T1D using validated psychometric tools.

Reference: Passanisi S, Bombaci B, Longo A, Alibrandi A, Salzano G, Lombardo F. The psychological impact of time in tight range in adolescents with type 1 diabetes: insights from real-life clinical practice. *Diabetes Research and Clinical Practice*. 2026;233:113160. doi: 10.1016/j.diabres.2026.113160

Note: The ISPAD–Breakthrough T1D Research Fellowship 2025 is acknowledged in this publication.

Study Design and Population

This cross-sectional study consecutively enrolled 123 adolescents with T1D (mean age 16.2 ± 1.8 years; mean diabetes duration 7.4 ± 3.6 years) during routine follow-up visits. The majority of participants (74.0%) used an AID system. Two validated psychometric instruments were administered: the Problem Areas in Diabetes - Teen Version (PAID-T), measuring diabetes-related distress, and the PERMA questionnaire, assessing psychological well-being across five domains (positive emotion, engagement, relationships, meaning, and accomplishment). CGM data from the two weeks preceding each visit were collected from cloud-based platforms to calculate the full set of standard CGM metrics, including TITR (70–140 mg/dL) and TIR (70–180 mg/dL).

Key Findings

A significantly higher proportion of youth achieved TIR ≥70% compared to TITR ≥50% (67.5% vs. 54.5%, p = 0.036), confirming that TITR represents a more demanding target even in a technologically advanced cohort.

The central finding was a significant positive association between achieving TITR ≥50% and higher diabetes-related distress as measured by the PAID-T score. This association was present in both univariate (OR = 1.018; 95% CI 1.002–1.034; p = 0.028) and multivariate logistic regression models adjusted for sex, age, BMI, diabetes duration, and treatment type (OR = 1.023; 95% CI 1.002–1.044; p = 0.029). Notably, no such association was found for the conventional TIR ≥70% target, suggesting that the two glycemic metrics carry distinct psychological implications.

Importantly, TITR achievement was not associated with differences in overall psychological well-being as captured by the PERMA model, indicating that the increased distress does not translate into a reduction of broader psychological well-being.

Relevance to the Fellowship Trial

These findings provide important preliminary evidence for the fellowship project. First, they establish that TITR ≥50% is associated with measurable psychological burden in a real-world cross-sectional setting, motivating the need for a longitudinal study to better characterize this relationship. Second, they validate the choice of the PAID-Teen as a primary psychological outcome in the fellowship RCT.

3. Concurrent Research Activities

In parallel with the fellowship project, several research activities were carried out during this reporting period, reflecting the breadth of my engagement within the pediatric diabetes research community.

3.1 Visiting Researcher, University of Cambridge

During part of the reporting period, I was based at the Department of Paediatrics, University of Cambridge, where I conducted clinical research on a pediatric cohort with early-stage T1D. This experience provided valuable exposure to longitudinal cohort methods, biomarker research, and international collaborative research networks. An abstract summarizing this work has been submitted to the ISPAD Annual Conference 2026.

3.2 CGM Metrics and Nerve Conduction Studies

A multicenter observational study investigating the association between CGM-derived metrics, including TITR, and nerve conduction study (NCS) findings in children and adolescents with T1D has been completed. The manuscript has been submitted for publication, and an abstract has been submitted to the ISPAD Annual Conference 2026.

3.3 Long-Term Real-World Use of an Automated Insulin Delivery System

A national multicenter observational study on the long-term use of an AID system over a three-year follow-up period has been finalized. The manuscript has been submitted for publication, and an abstract has been submitted to the ISPAD Annual Conference 2026.

3.4 Indirect Indexes of Insulin Resistance in Adolescents with T1D

A multicenter observational study examining indirect markers of insulin resistance in adolescents with T1D is currently ongoing. Data collection is in progress across multiple Italian centers.

3.5 JENIOUS/ISPAD International Survey on Smart Insulin Pens

As part of my role within the JENIOUS Group of ISPAD, I am leading an international multicenter survey on the use of smart insulin pens in children and adolescents with T1D. The survey, designed and distributed through the JENIOUS network, is currently ongoing and aims to characterize current practices, perceived advantages, and barriers to adoption of this technology across different healthcare settings worldwide.

4. Next Steps

For the second half of the fellowship, the planned activities are:

- Full activation of participant recruitment at the Pediatric Diabetes Unit, AOU “G. Martino”, Messina, with the goal of reaching the target sample size.
- Baseline data collection, including demographic and clinical variables, CGM data, HbA1c, and psychological questionnaires.
- Follow-up visits with enrolled participants, with systematic download and review of CGM data.
- Preparation of an abstract based on preliminary data for presentation at upcoming international conferences.
- Completion of data analysis and manuscript preparation.

5. References

1. Shah VN, DuBose SN, Li Z, et al. Continuous glucose monitoring profiles in healthy nondiabetic participants: A Multicenter Prospective Study. J Clin Endocrinol Metab 2019;104:4356–4364.

2. Battelino T, Alexander CM, Amiel SA, Arreaza-Rubin G, Beck RW, Bergenstal RM, et al. Continuous glucose monitoring and metrics for clinical trials: an international consensus statement. Lancet Diabetes Endocrinol. 2023;11(1):42-57.

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